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INTRAVITREOUS STREPTOMYCIN: ITS TOXICITY AND DIFFUSION*

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THE discovery of the new antibiotic, streptomycin, by Waksman and his colleagues in 1944, has put at our disposal a substance capable of producing a chemotherapeutic action on organisms not particularly susceptible to other agents. Gram negative organisms and M. tuberculosis are the organisms for which streptomycin is particularly effective. Previous work has shown that streptomycin does not easily penetrate through the cornea (Leopold and Nichols, 1946) and it was decided to investigate the concentrations of the

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drug attained in ocular fluids following its administration (1) into the vitreous and (2) subconjunctivally. It is known that drugs injected into the vitreous may produce damage, sometimes severe, to the retina (Duguid *et al.*, 1947) and an investigation of the action of streptomycin on the eye tissues following its intravitreous administration was therefore also undertaken. The results of Bellows and Farmer (1947) published in the meantime would suggest that streptomycin is non-toxic to the retina and can safely be administered by the intravitreous route.

Methods

Two samples of streptomycin were used in these experiments and we are greatly indebted to the Antibiotics Study Section of the U.S. Public Health Service (through Dr. Seger) for supplying these. The pure sample was used for the intravitreous toxicity tests; it was streptomycin hydrochloride calcium chloride double salt (Pfizer lot X 76), and its biological activity against B. subtilis was 719 u/mg. For the diffusion experiments the second sample of commercial streptomycin (Merck) was used.

For the diffusion experiments 2,000 μg. of streptomycin was injected into the vitreous in 0·1 ml. of sterile saline by the method previously described (Duguid *et al.*, 1947). For the toxicity experiments two doses were used, *viz.*, 1·2 mg., and 3·0 mg., injected in 0·1 ml. saline. In these latter experiments the eyes were observed at regular intervals for periods of 12 to 112 days and the changes noted. The eyes were then removed and examined histologically.

The method for assaying streptomycin in the aqueous and vitreous was based on the measurement of the diffusion of streptomycin through agar. The melted nutrient agar (Stebbins and Robinson, 1945) was seeded with a 24 hour culture of the Mayo Clinic strain of staph. aureus to a final dilution of 1/1000 and added to a series of glass tubes. After the tubes had cooled for five minutes small quantities of the eye fluids for assay were added above the agar. Four tubes were used for each eye fluid. The tubes were incubated at 37° C. for 24 hours and the zone of inhibition between agar-eye fluid and line of growth was measured in millimetres. The measurements were made by fixing a tube on to a slide, placing it on the mechanical stage of a microscope, and viewing the zone of inhibition through a 2/3 inch objective with a pointer attached. The transverse millimetre scale gave readings to the nearest 0·1 mm. With suitable controls of 2 and 64 μg. per ml. a graph was constructed from which the unknown fluids were estimated.

It was shown that streptomycin control solutions made up in saline gave identical zones of inhibition to those made up in buffered aqueous or vitreous and so the former were used for convenience throughout. The method is much more reliable if the fluids for assay are kept alkaline. All ocular fluids were therefore diluted with an equal quantity of m/10 phosphate buffer at pH 7·8 before assaying.

The method is accurate to within ±20 per cent. and gives a reading down to 0·5 μg. per ml. Even small quantities of 0·2 ml. of aqueous are sufficient for four estimations by this method.

The concentration of streptomycin in aqueous and vitreous was measured, by the above method, 24, 48 and 72 hours after the injection of 2,000 μg. streptomycin in 0·1 ml. sterile saline into the vitreous (see Table I).

TABLE I

Concentration of streptomycin after intravitreous injection of 2,000 μg streptomycin.

Time after injection, hours	Rabbit Number	Concentration of streptomycin (μg. ml.)	
		Aqueous	Vitreous
24	36* R. Eye	41	—
	L. Eye	<0·5	—
	37* R. Eye	84	—
	L. Eye	<0·5	—
	38 R. Eye	43	340
	39 R. Eye	46	200
	40 R. Eye	86	215
48	41 R. Eye	20	—
	42 R. Eye	34	—
	43 R. Eye	24	—
72	44 R. Eye	12	—
	45 R. Eye	13	—

* Right eye only received streptomycin injection.

In another smaller series the concentration of streptomycin in the aqueous was measured 3, 6 and 24 hours after subconjunctival injection of 10,000 μg. streptomycin made up to a total volume of 0·2 ml. in 1/1000 adrenalin (see Table II).

TABLE II

Concentration of streptomycin after injection of 10,000 μg. in 1/1,000 adrenalin subconjunctivally.

Time after injection, hours	Rabbit Number	Concentration of streptomycin (*μg. per ml.*) in aqueous
3	1	20
	2	8
6	3	0·8
	4	0·5
24	5	<0·5
	6	<0·5

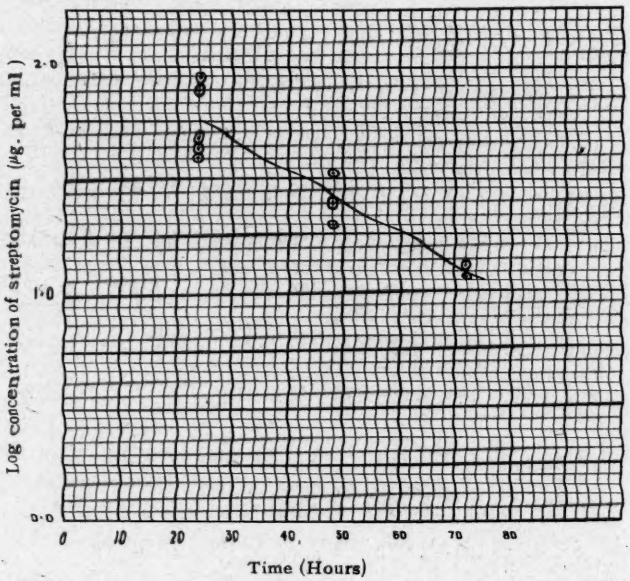

FIG. 1.

Concentration of streptomycin in aqueous after intravitreous injection of 2,000 ug. of *streptomycin*. *Aqueous-vitreous* ratio at 24 hours=0·25.

For the toxicity experiments streptomycin was injected into the vitreous of the right eyes of five animals while as a control 0·1 ml. of normal saline was injected into the vitreous of the left eye in each case. One animal received seventeen doses of streptomycin subconjunctivally over a period of 20 days, when the globe was examined histologically.

Results

1. *Diffusion of streptomycin.*

The results are given in Tables I and II and shown graphically in Figs. 1 and 2. It will be seen that after the intravitreous injection of 2,000 μg. of streptomycin, this acts as a depot and chemotherapeutic concentrations are maintained in the ocular fluids for over three days. The diffusion of streptomycin is therefore appreciably slower than that of penicillin, the data for which (previously described by Duguid *et al.*, 1947) are also shown in Fig. 1, A.

On the other hand the subconjunctival injection of a larger dose

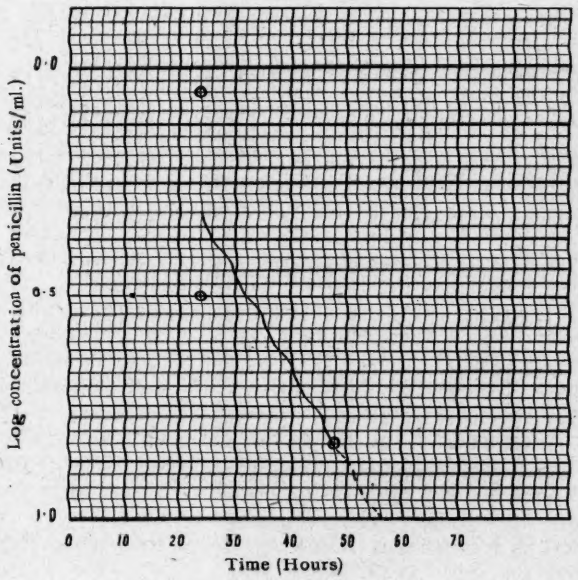

FIG. 1A.

Concentration of penicillin in aqueous after intravitreous injection of 2,000 units of penicillin. Aqueous-vitreous ratio at 24 hours=0·01.

of the drug (10,000 μg.) combined with adrenalin to delay the rate of absorption produced a chemotherapeutic concentration in the aqueous for only a short period (Fig. 2).

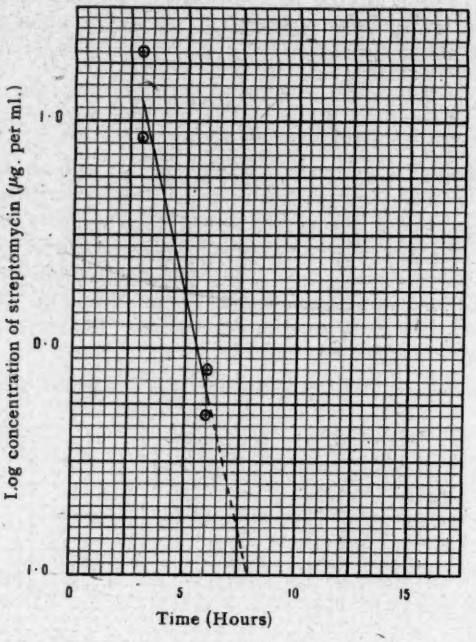

FIG. 2.

Concentration of streptomycin in aqueous after subconjunctival injection of 10,000 μg. of streptomycin in 1/1000 adrenaline.

2. *Toxicity of streptomycin.*

Five animals were injected with streptomycin. Two of them (128 and 129) received 1·2 mg. in 0·1 ml. saline into the right eye and 0·1 ml. saline into the left (control) eye. The periods of observation were 77 and 112 days. The other three (130, 131 and 132) received 3·0 mg. in 0·1 ml. saline into the right eye and 0·1 ml. saline into the left eye. The periods of observation were 12, 77 and 112 days.

The retinal changes following the intravitreous injection of streptomycin were pronounced.

The two eyes which received 1·2 mg. showed only trifling and transitory immediate oedema but pigment stippling was extensive after one week in one and after two weeks in the other. Both

showed patchy retinal atrophy in the region of the disc and medullated fibres, about a week after the pigment stippling appeared. The globes after fixation were bisected in front of the ora serrata and the lesions noted clinically identified with the help of the slit-lamp. The affected portions of the fundus were excised, embedded in paraffin and the sections stained with haemalum and eosin. In one fundus there can be noted a gross loss of the cellular elements of the retina over a large area with migration of pigment into it from the hexagon pigment layer. In the other eye there is over a large area a disturbance and loss of the outer retinal elements. In neither case does the choroid appear to be affected. The larger dose (3·0 mg.) produced even more distinctive changes. In one (131) the whole inferior retina became atrophic after a period of oedema followed by pigment changes. The other two animals (130 and 132) showed deep oedema immediately after the injection and shortly afterwards widespread pigment reticulation began to be noticeable. Histological examination of the three eyes receiving the larger dose shows in all of them extensive loss of all retinal elements over large areas with massive pigment infiltration of the retina. In one eye the retina was almost completely detached.

In the retina of the eye which received subconjunctival injections of streptomycin no changes were found, either clinically or histologically.

One control eye showed some exudate in the central third of the inferior periphery of the retina. The vitreous of the other eye had been injected with 3·0 mg. streptomycin.

Summary of the toxicity experiments

It is clear that streptomycin has a deleterious effect on the retina when it is introduced into the vitreous in doses of 1·2 or 3·0 mg. It would not appear to have any toxic effect on the fundus when given subconjunctivally.

Discussion

After a single intravitreous injection of 2,000 μg. of streptomycin an effective therapeutic concentration was maintained in the ocular fluids for at least three days. This slow rate of diffusion of streptomycin is similar to that obtained by Bellows *et alü* (1947) using 25 to 100 μg. of streptomycin per injection. From this point of view a single intravitreous injection of streptomycin might well be sufficient to deal with certain ocular infections in man.

On the other hand the present findings show clearly that even

1·2 mg. (863 μg. of activity) of pure streptomycin produces serious and permanent retinal damage. These observations are at variance with those of Bellows *et alii* (1947), who showed that intravitreous streptomycin in amounts of 25 to 1000 μg. per injection failed to give rise to any permanent damage to the fundus. Their series of experiments was done using solutions of various commercial lots and a purified sample of streptomycin and were also followed by ophthalmoscopic and histological examinations. Our toxicity series was done on a pure sample of streptomycin (Pfizer X 76) and we have seen similar changes with the ophthalmoscope in eyes injected with commercial streptomycin. The difference between these findings may well be due to differences in the toxicity of the streptomycin used, but the data suggest that at present great caution should be used in the intravitreous use of streptomycin.

Summary

(1) Intravitreous injection of 2,000 μg. of streptomycin acts as a depôt from which streptomycin diffuses away slowly, chemotherapeutic concentrations still being present in the ocular fluids after three days.

(2) The toxic effects of streptomycin introduced into the vitreous in dosages of 1·2 and 3·0 mg. result in marked retinal damage.

We are grateful to the W. H. Ross Foundation (Scotland) for the Prevention of Blindness who have defrayed part of the expenses of this work.

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AN ANALYSIS OF FIBRE-SIZE IN THE HUMAN OPTIC NERVE*

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DATA on the fibre-size " spectrum " in the optic pathways must form an essential anatomical preliminary to electro-physiological studies of the visual neural system. Extensive studies on peripheral nerves have brought to light some of the factors on which the differences of calibre of nerve fibres appear to be based. Studies of fibre-size in the central nervous system have been carried out by Häggquist (1936) on the spinal cord, and by Szentágothai-Schimert (1941) on several of the important pathways of the brain.

It has been recognised from the time of Gudden (1886) that the optic nerve contains myelinated fibres of graded size. Arey and his co-workers in their extensive investigation on the quantitative (and to a certain extent qualitative) composition of the optic nerve in a series of vertebrates, observed that in man all the fibres are myelinated and are of widely varying size. A considerable body of electro-physiological work on the optic nerve has been completed on frogs, rabbits and cats, and attempts have been made to group the fibres in this nerve on a physiological basis using conduction rate, threshold to electric stimuli, refractory period, time to maximum, etc., as criteria for grouping. In the histological study which this work entailed the authors arbitrarily distinguished certain fibre-sizes and attributed to them certain physiological properties. As yet, however, no systematic analysis of the range and frequency of the fibre-sizes in the optic nerve has been attempted. The importance of this investigation is emphasised by the findings of Granit that the electrical activity in the optic nerve (as recorded from its constituent fibres by his micro-electrode technique) indicates a specific sensitivity of the related receptors and their associated neurons in the retina to monochromatic lights. Such elements in the retina, possessing specific sensitivity to different wave-lengths of light, will give rise to impulses which are probably conducted along nerve fibres of one particular type in preference to others. The qualitative variations of nerve fibres so far recognised are the varying thickness of the axis-cylinder and of the myelin sheath, and the presence or absence of the sheath of Schwann and the nodes of Ranvier. The present investigation deals with fibre-sizes, which are analysed in detail.

Material and methods

Human optic nerve sections of 5μ thickness were prepared and several standard silver and myelin stain techniques were employed.

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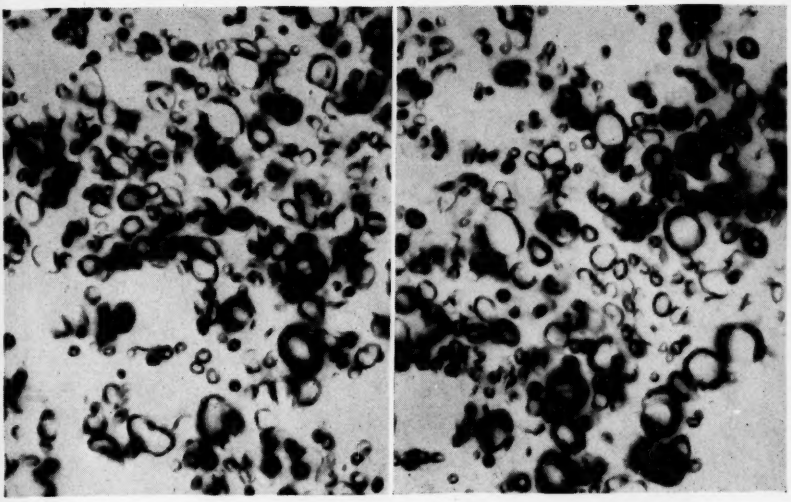
Of these, Weigert-Pal preparations were found most suitable for measurement, while the others were used for the purpose of checking and confirmation. The particular specimen which was used for measurement was the optic nerve of a man, aged 61, in whom no defective vision or any other affection of the visual system was reported. No reduction in the size of the fibres of the central nervous system is apparent at that age according to the report of Szentágothai-Schimert (1941).

In order to measure the diameter of the fibres and to group them simultaneously, a method was devised (Allison and Chacko, 1948) in which an Abbé camera lucida was used to superimpose the image of a scale with lines of graded thickness corresponding to the range of size of the nerve fibres in the optic nerve. The scale is so prepared and calibrated that when the width of a line coincides in its image with the diameter of a nerve fibre it indicates the actual diameter as well as the size-group to which it belongs. Thus, it is possible to arrange the fibres into groups of smaller range than those adopted by Häggquist or Szentágothai-Schimert. A square corresponding to $(60\mu)^2$ area of the microscopic field and containing 25 small squares each $(12\mu)^2$ was drawn and fixed under the mirror of the camera lucida. The nerve fibres in each small square were measured one after the other and ticked off. From the average number of fibres within the area $(60\mu)^2$ the total number of fibres in the optic nerve was also estimated in the usual way.

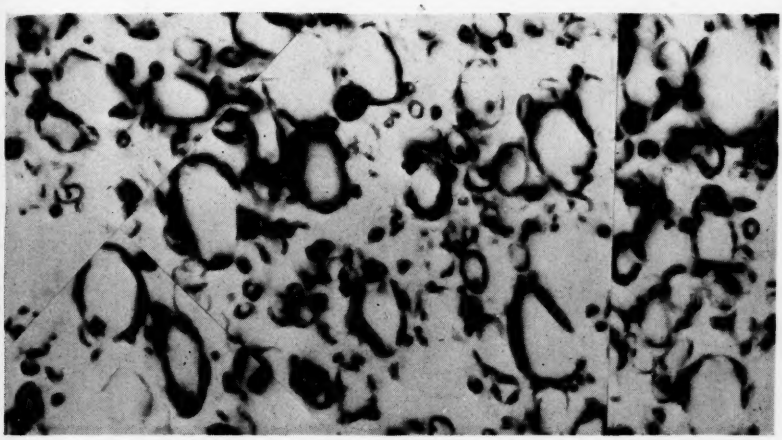
It was found that in a well-prepared section the myelin rings are undistorted and in fibres cut transversely appear as smooth circles. However, in their course through the optic nerve, the constituent fibres undergo a certain amount of rearrangement and in cross-sections of the nerve, many fasciculi may be seen running a more or less oblique course as they change their relative positions. Such fibres appear in sections as oval or rod-shaped, and in this case it was decided to take the short diameter as approximating to the true diameter of the fibres. The total diameter of the fibres (including the myelin sheath) was measured in each case. Measurements of about 4,000 fibres contained in fifteen fields of $(60\mu)^2$ along eight radii of the cross-sectional outline of the nerve were taken and grouped in $\frac{1}{2}\mu$ ranges. The frequency percentages of these groups were then calculated and a histogram was drawn.

Results

The human optic nerve contains fine, closely packed, myelinated fibres without Schwann sheaths; these fibres exhibit a continuity in range of size from the smallest to the largest diameter (Fig. 1). The minimum calibre measured was $0{\cdot}7\mu$ and the maximum $8{\cdot}0\mu$, and very occasionally fibres of $10{\cdot}0\mu$ sizes were also noted (Fig. 1*c*). The histogram (Fig. 2) shows that the greatest frequency of the fibres is under $1{\cdot}0\mu$ and the next greatest from $1{\cdot}0$ to $2{\cdot}0\mu$, at which



a *b*



c

FIG. 1.

Microphotographs of Weigert-Pal preparations of the optic nerve in man. Magnification ×1000. (*a*) Note the variation in the sizes of fibres, their distribution, and the predominance of small fibres of about 1μ size. (*b*) In this particular region fibres of 4-6μ size appear in greater number. (*c*) Microphotograph of the same preparation from regions where large fibres of about 10μ form the outstanding feature.

level the frequency drops rather steeply towards the base line and then more gradually in the direction of the larger fibres with an indication of a second low rise in the region of 5·0 to 7·0μ. This last feature was more pronounced in confirmatory measurements carried out from other preparations.

Minute " dots and rods," mentioned by Brodal and Harrison (1948) as indicative of the possible existence of minute myelinated fibres in the central nervous system, were not particularly evident in any of our preparations although their presence could not be positively excluded. Moreover, the continuous range that characterises the sizes between 0·7μ and 8·0μ did not extend below 0·7 down to the sizes indicated by " dots and rods " that may be present. The total number of optic fibres in the human optic nerve was estimated to be between 815,000 and 1,000,000 fibres.

Comments

The histogram of the fibre-calibre of the optic nerve corresponds very roughly to the first of the two peaks of the fibre size histogram.

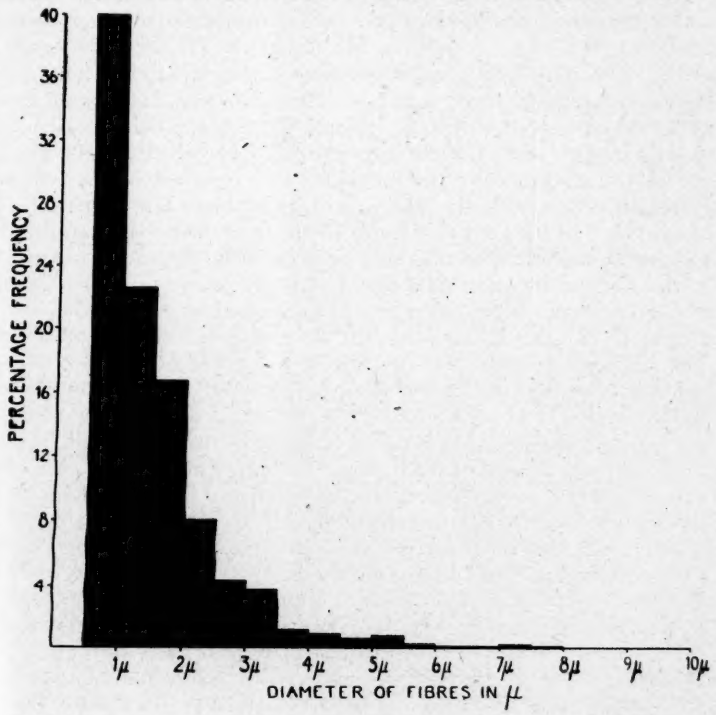


FIG. 2.

Histogram of the percentage distribution ofa bout 4000 nerve fibres of various sizes in the human optic nerve

in somatic motor (Häggquist, 1937) and somatic sensory nerves (Szentágothai-Schimert, 1941), with the difference that the maximum is shifted to the left, showing a much higher frequency in the under-2μ range. It approximates more closely to the range and frequency in visceral nerves. There is a closer comparison, however, between the height and position of the maximum in the optic nerve histogram and that of the pyramidal pathway in the basis pedunculi which, as shown in the investigation of Szentágothai-Schimert, is due to the inclusion in it of cortico-pontine fibres. The picture of the ponto-cerebellar tract is also similar (Szentágothai-Schimert 1941).

The second much smaller maximum at about 5-7μ may also be significant in view of the possibility that these fibres are related to the larger cell layers of the lateral geniculate body.

Polyak (1942) has observed that the optic fibres proceeding from the periphery of the retina towards the optic disc are thicker than those from the macula. He also points out that the larger ganglion cells are more numerous towards the periphery of the retina and small ganglion cells towards the area centralis and that, generally speaking, the larger cells send out thicker axons than the smaller cells. The possibility may be conjectured, therefore, that the disproportionately large number of fine fibres in the human optic nerve (as compared with other mammals) proceed mainly from the small ganglion cells, possibly from the midget ganglion cells which are in the majority in the macula. The increase in the midget ganglion cells and their related midget bipolars and cones in the central area of the retina (Polyak 1942), the relative increase in the number of fine fibres of the optic nerve, and the remarkable increase in the number of small cells in the central vision area of the lateral geniculate body in the ascending phylogenetic series (Chacko 1948), appear to be consequent upon the differentiation of central vision. The higher frequency of fine fibres, the great number of monosynaptic connections and neurons of smaller size in contrast to thicker fibres, converging pathways and larger neurons are interesting features of the visual neural system. If the suggestion proves to be correct, that the nerve fibres forming the macular pathways from the retina to the cortex are of relatively smaller calibre, then the current idea that the relatively thicker and fast-conducting fibres convey impulses destined for the visual cortex, while the thinner slow-conducting fibres only reach the tectum, will need to be revised. However, increase of fibre diameter is only one of the factors related to a higher conduction velocity (Young 1946). An alteration of the histochemical properties of its sheath may have the same result. As is clear in Fig. 1, the fine fibres have a distinct myelin sheath, but there is a relatively greater thickness of myelin sheath in the finer fibres. The nature of the sheath in these fine fibres is well worth study with the technique of polarization optics and X-ray diffraction analysis. Histograms of the optic

nerve fibre-calibre in clinical cases of toxic amblyopia where the macular bundle is mainly affected, or in experimental lesions of the macula, and also a comparative study of the normal histograms in a series of primates and sub-primates, should throw further light on the subject; work along these lines is in progress.

I wish to thank Prof. W. E. Le Gros Clark for encouragement and advice while carrying out this work.

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ACUTE RETINOPATHY WITHOUT HYPERPIESIS IN DIABETIC PREGNANCY*

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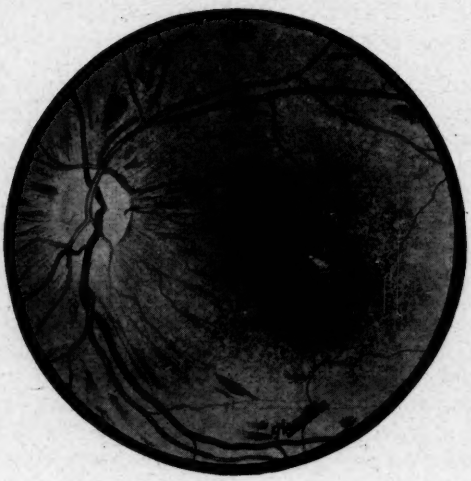
I HAVE recently seen acute haemorrhagic retinopathy in two pregnant diabetic women such as has not hitherto been described. Retinopathy is all too common in *long-standing diabetes*, but is a slow process with characteristic venous haemorrhages and exudates developing slowly over years, although a form which quickly develops into retinitis proliferans is occasionally seen. The severe *toxaemia of pregnancy* too produces an acute retinopathy with oedema, papillitis, severe haemorrhages, " albuminuric " in nature and appearance, always associated with hypertension, albuminuria and toxaemia. The following two cases fall into neither of the above categories, have not been described in ophthalmology or diabetic literature and presented a novel problem as to the termination of these pregnancies. The condition must be very rare and I have seen it in only 2 of some 200 diabetic pregnancies closely followed and is so striking in visual defect that I could not have missed other such cases.

* Received for publication, March 19, 1948.

CASE 1. A very long-standing case who developed diabetes at age of 11 years in 1924, had insulin for 19 years before her pregnancy in 1943 at the age of 30 years. She was a spirited and clever young woman who led the wildest of diabetic lives, travelling all over the world on insulin varying from 20 to 80 units a day,

CASE 1.



CASE 2.

often loaded with sugar and ketones, precomatose from short supplies of insulin in the Tropics and a perfect candidate for retinal and other complications which long-standing and especially uncontrolled diabetes often brings. Married in 1942, after a miscarriage at 3 months, she again became pregnant and when seen at 10 weeks determined to co-operate in every way and rest and progesterone were followed. Her eye grounds and general physical state were normal. At 20 weeks, after a few days of mild sickness and vomiting, misty vision developed and when she was admitted for observation at the 23rd week, severe haemorrhagic retinopathy and a little exudate were obvious. Mr. Savin's notes gave the following details (December 1943). " Very extensive bilateral retinopathy with macular oedema and some exudate at L. macula. There are numerous flame-shaped and circular retinal haemorrhages. The vessels do not seem badly affected; no swelling of the discs. This is a serious haemorrhagic retinopathy. I could not be at all sure ophthalmoscopically if it were diabetic in origin and have no experience of the effect (nor necessity) of terminating pregnancy." (See Fig. 1.) Several other physicians and ophthalmologists confessed their ignorance. I had expected perhaps some renal toxaemia, but every *urinary* and *blood* test was *normal* (blood pressure 110/70 as always). After this her vision improved a little but when seen at the 30th week, her eye grounds were the same except for less macular oedema. After this, war conditions made London difficult and a healthy child was produced by Caesarean section in her home town at the 37th week. Her vision improved (" normal," she said) but one year later (1945) I saw two typical diabetic punctate haemorrhages, a big dilated venule, a small white exudate and some fading haemorrhages at the right macula. After another year (April, 1946) a report from Mr. N. P. R. Galloway said that although her vision is 6/6, 6/5, her right fundus shows fine vitreous veils like commencing retinitis proliferans and the left, a few punctate haemorrhages, typical of diabetic trouble. Before this she again became pregnant, but abortion was induced. So a retinopathy still persisted, seemingly diabetic. When examined 18 months later, however, 5 years after the original lesion, the fundi were entirely normal.

CASE 2 had a very similar early history. Diabetes began at the age of 10 years in 1930, much insulin—60-80 units—often too much food and gross obesity. First pregnancy in 1943, normal child by Caesarean section, normal eyes.

A *second pregnancy* (1946) began normally and the eye grounds remained normal until " influenza " with 4 days' severe *vomiting* occurred at the 28th week, followed at once by " misty and spotty " vision. When seen a week later an intense haemorrhagic retino-

pathy was present and Mr. Savin reported: " She has a severe bilateral haemorrhagic retinopathy with numerous flame-shaped and deep haemorrhages and a little exudate. The peripheral arteries are in many instances narrowed and in a state of spasm. Discs normal. In my view this is a toxic condition rather than the type usually associated with diabetic retinopathy." However, all tests for toxaemia in blood and urine were normal, blood pressure 110/60, very slight anaemia, B.S.R. 34 mm./1st hour. RH factor positive, no atypical antibody. Arm capillary fragility normal. Altogether nothing abnormal was found except the diabetes. Vitamin K and B_1 were given in large doses. In the next weeks bilateral Bell's Palsy developed and the retinopathy became slightly worse (see picture by Messrs. Hamblin). Nausea and occasional vomiting continued. Termination was most seriously considered, but the mother instinct settled our problem by refusal. The vision fluctuated for better and worse, more haemorrhages, more and less oedema.

After Caesarean section at the 32nd week the vision became " normal " within a week and we watched the haemorrhages fade. Six months later Mr. Savin reported " the retinae and vessels are normal apart from some faint pigmentary patches and 1 or 2 crystalline deposits, relics of previous haemorrhages. But all this is a mere trifle."

I, however, saw *one* deep punctate haemorrhage, to me typically diabetic, in the left eye ground. But all the acute haemorrhagic process had certainly gone and the eye grounds had returned practically to normal. A year later the fundi were normal.

Discussion

I have not been able to find any similar published cases. In contrast I have followed 3 pregnancies in 2 diabetic women who previously had slight retinopathy, a few haemorrhages and fleck exudates, and the course of pregnancy made no difference to their retinal condition. Also I have followed about 12 diabetic pregnancies complicated with renal toxaemia, usually mild, which showed no retinal changes.

The only common factor in these two pregnancies different from many similar long-standing cases was unusual vomiting. This certainly raises the venous pressure and might well put the extra rupturing strain on the venules which are known to be the weak point in the diabetic retinal system. It is to be remembered also that the intra-ocular pressure is certainly reduced by dehydration, this diabetic disturbance being present in all such states of vomiting in severe insulin cases. But even if these two factors are causal ones in this retinopathy, it is hard to see why the condition should

persist almost unchanged until delivery. So perhaps it is wise to report these two cases without explanatory hypothecation.

Summary

Two cases of acute and severe haemorrhagic retinopathy are described in pregnant diabetic women. The condition does not conform either to usual diabetic or to toxic renal retinopathy and the latter was excluded.

I am indebted to Mr. L. H. Savin for close study and reports on the retinal changes.

CRATER-LIKE HOLES IN THE OPTIC DISC*

BY

EMANUEL ROSEN

NEWARK, N.J.

ALTHOUGH Duke-Elder[1] has stated that the condition known as " pits " or " crater-like holes in the optic disc " is of relatively frequent occurrence, yet Greear[2] has been able to collect and tabulate only seventy-two cases including his three cases, the only three he had encountered in eighteen years of active practice. There would seem to be sufficient reason to report any additional cases and possibly in so doing to lend statistical support to the present-day concept of the condition without the necessity of awaiting pathological studies before one can be sure of the nature of this anomaly[3].

CASE 1. This 31-year-old patient was examined routinely prior to embarkation. His vision was 20/20 in each eye and his only ocular complaint was difficulty in reading for prolonged periods. There were no abnormal eye findings other than those of the right disc (Fig. 1). This disc was ovoid in shape with a thin, pigmented scleral ring on the temporal side. There was present a small physiological cup about 1/3 D.D. in size located slightly upward and nasally. The cup was about three dioptres in depth and presented a pronounced cribriform plate at its bottom. Just nasal to the physiological cup was a triangular-shaped " pit " with its apex pointing inferiorly. This " pit " did not reach quite to the edge of the disc nor to the nasal edge of the physiological cup. The " pit " appeared to be blue-grey in colour and seven or eight dioptres in depth. A thin connective tissue veil seemed to be present within the cup rendering it difficult to visualize the bottom

* Received for publication, March 4, 1948.

of this " crater." The edges of the " crater " were quite distinct. One small vessel could be seen approaching the nasal side of the disc and then disappearing over the nasal lip of the " pit." This vessel could not be followed very far down into the " pit " for it

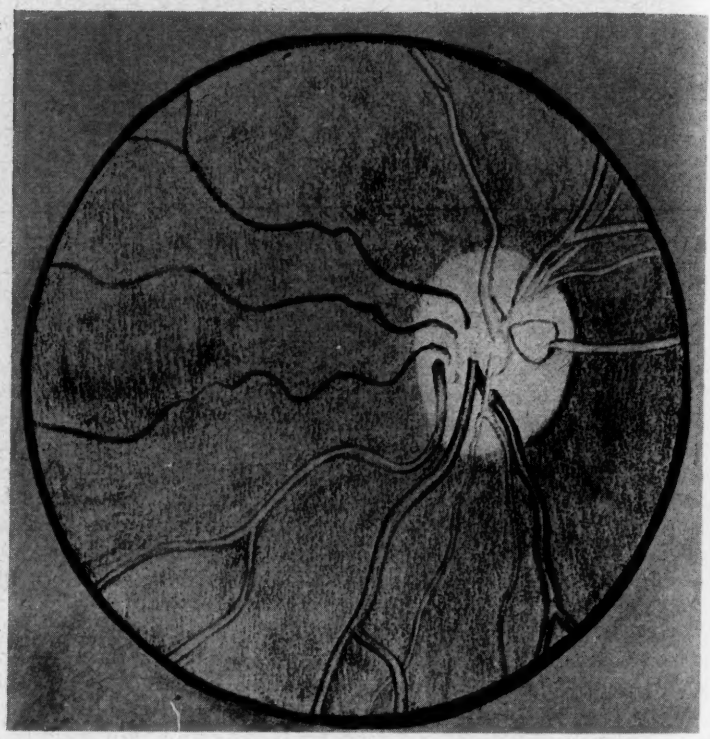


FIG. 1.

seemed to disappear completely. There was no further anomaly of structure of this disc. The patient's vision was found to be 20/20 in each eye with correction. Fields and blind spot studies produced the pictures seen in Figs. 2 and 3.

In summary this disc presented a " pit " upon the inferior nasal aspect of the disc triangular in shape and seven or eight dioptres in depth. A temporal crescent was present along with a characteristic field defect. The " pit " was covered over by a connective tissue substance and was blue-grey in colour.

CASE 2. The second case was that of an adult male, aged 51 years, who appeared for a routine refraction and offered the information that he had upon a previous examination been informed that there was present in his right eye a very rare condition known as a " hole in the optic nerve." After learning of this condition the

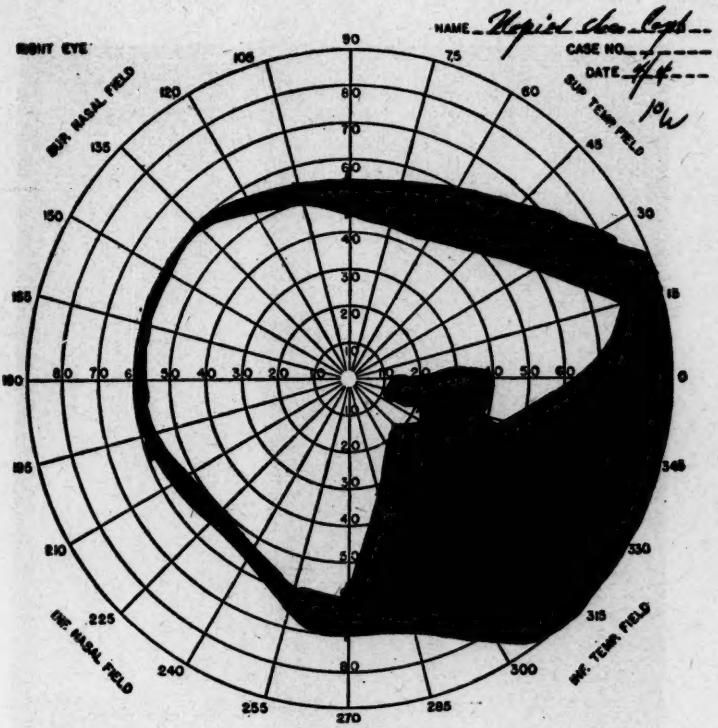


FIG. 2.

patient had conducted several tests upon himself in which he learned that he had a field defect in his right eye which to him seemed quite marked when compared with the visual field of his left eye.

Examination of the left eye was not remarkable. The right eye too was not unusual, except for the appearance of the right disc (Fig. 4). This showed a pigmented greyish-black scleral crescent upon the nasal third of the disc which was fairly well demarcated in its upper half but not pigmented below. There were three islands of clear area within the crescent. A fairly large physio-

logical cup was present which occupied about one-third the entire area of the disc and was eccentrically displaced nasally. The central retinal vessels emerged in no unusual manner from this cup with the primary arterial and venous bifurcation occurring before emergence. On the temporal portion of the disc a very small round " pit " was present which approached but did not

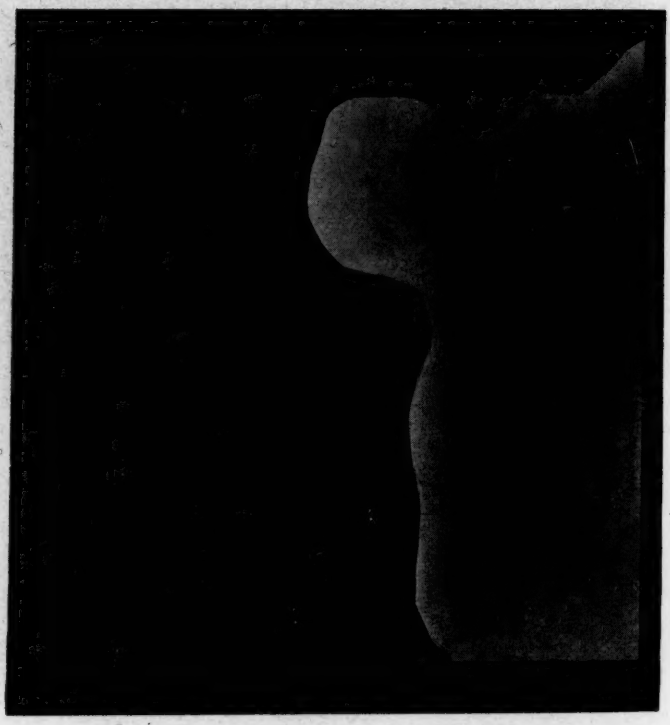


FIG. 3.

touch either the physiological cup or the disc margin. One small vessel appeared to enter the cup near the upper edge, emerging at approximately " 9 o'clock " and running upward over the disc edge. Below the lower lip of the " pit " a small vessel approached the edge of the hole but then curved gracefully away to run off the disc and on to the retina. The " pit " was of pale blue colour and was covered over by a greyish foam-like membrane so that the depth of the hole could not be ascertained. The hole seemed to

take a slightly oblique source temporally. There were no other anomalies of the vessels upon the disc or the retinal structures. A study of the visual field disclosed a defect as pictured in Fig. 5.

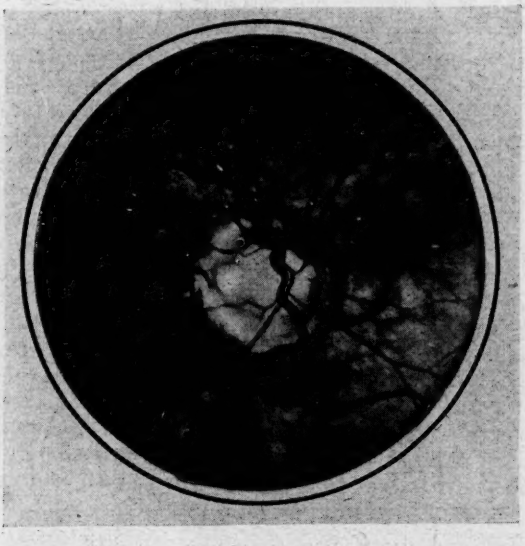


FIG. 4.

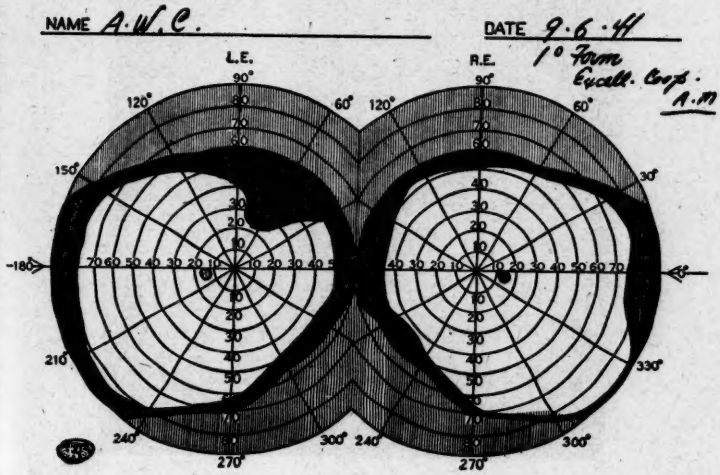


FIG. 5.

CASE 3. This patient, aged 29 years, was examined at this hospital because of extremely poor vision in his right eye of many years' duration. This eye had always been much poorer than his left eye and although the patient was right-handed he was aware of the fact that he had always used his left eye when sighting through a rifle. About ten years ago the right eye was injured by a small seed brushed from some tall grain. The patient was seen shortly afterwards by a specialist who removed a foreign body from the cornea and then put a patch upon his eye. When this patch was removed the patient noticed that his vision was greatly reduced. He doesn't recall making any effort to determine the cause of this diminished vision subsequently, but knows that at every eye examination thereafter something of interest was discovered in his right eye which caused a good deal of comment by all examiners. Examination disclosed vision in the right eye to be restricted to hand movements. The external ocular examination was negative. The right eye was slightly divergent; no effort was made at fixation. The iris and lens were normal. In the right macula there was a horizontal lesion resembling a tear with the prominent redness of the choroid brightly shining through and with the edge of this cleft strongly pigmented. There was a definite and complete scleral temporal crescent and in the infero-temporal portion of the disc was an obliquely placed slightly triangular

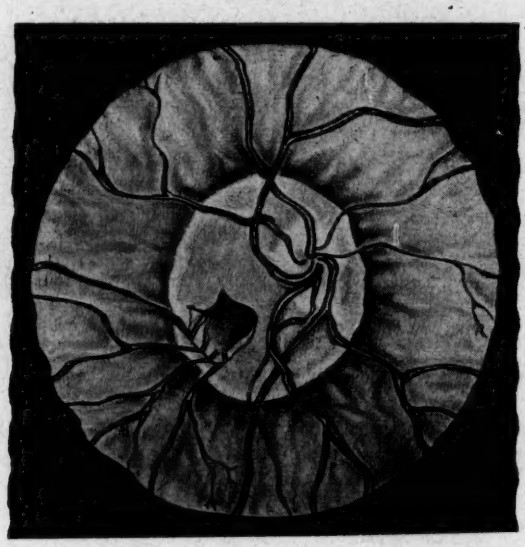


FIG. 6.

" pit " (Fig. 6). This was about 1/8 D.D. in size and was covered over by a rather dense connective tissue membrane which was somewhat shiny. The " hole " was greyish-blue in colour; its depth could not be measured since one could not focus beyond the range of the connective tissue covering. The temporal edge of the " pit " did not quite reach to the edge of the disc. Its margin temporally was extremely distinct and the oblique nature of the " pit " appeared to be emphasized by this sharp temporal edge. In the inferior portion a vessel seemed to approach the hole and then pull away from it without entering the " pit." There was a pronounced physiological cup with normal vessel arborization. A visual field study done upon this eye failed to illustrate the characteristic sector-shaped defect probably because of the extremely poor fixation resulting from the macular lesion. There was a marked concentric contraction of the peripheral field.

CASE 4. Is that of an adult male soldier 27 years who had been under the care of the eye department at a station hospital for more than a year because of suspected glaucoma. During a routine examination for refraction the peculiar cupped appearance of the patient's left disc was observed (Fig. 7). Following changes noted in the blind spot of that same eye, the patient was put upon an anti-glaucomatous régime. He was observed at very frequent

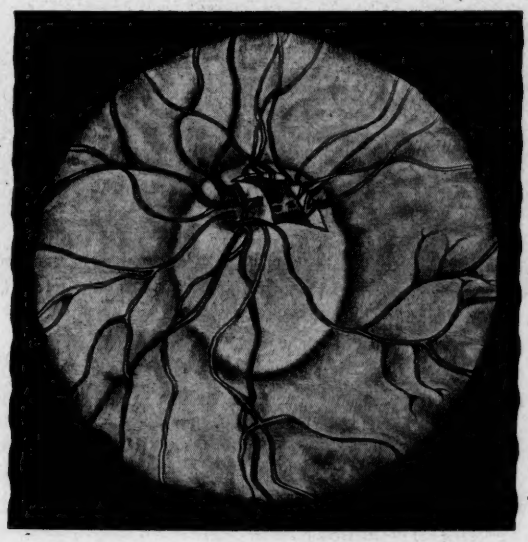


FIG. 7.

intervals during which time no variation was discovered in the appearance of the blind spots, the peripheral fields or the diurnal tension curve. Vision in each eye was 20/70 but was readily corrected to 20/15. There was no involvement of the peripheral field but studies of the blind spots showed an enlargement (Fig. 8).

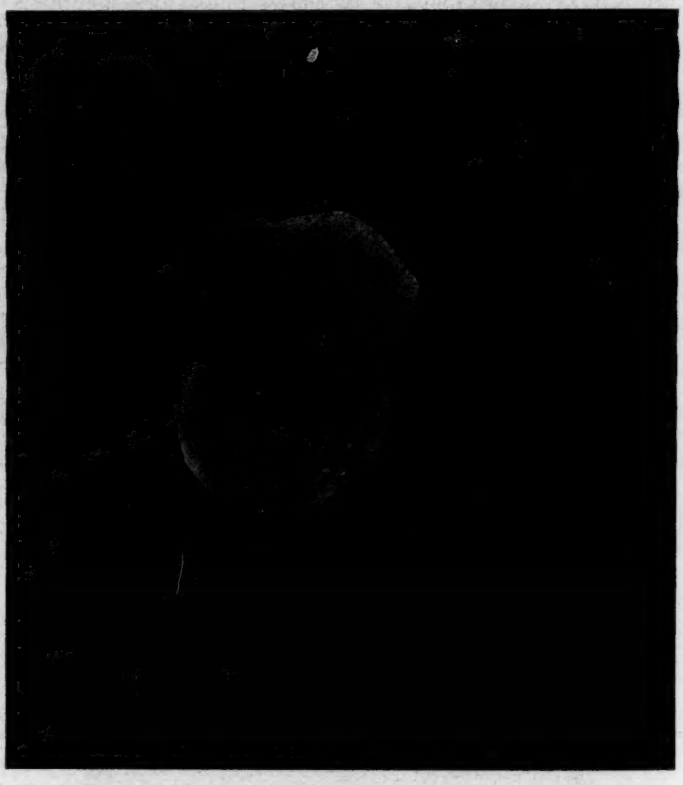


FIG. 8.

The fundus of the right eye presented a small colobomatous area just below the disc enclosed by a pigmented crescent and traversed by several retinal vessels which certainly suggested the presence and location of an atypical congenital coloboma (Fig. 9).

CASE 5. A. S., aged 10 years, had been given occlusion therapy because of an amblyopic left eye. This consisted of total occlusion during the summer months and occlusion therapy several hours daily after school. The treatment was continued for a period well

over one year at the end of which time no improvement was noticed. The patient was first seen shortly thereafter. During routine fundus examination a crater-like " pit " in the optic disc

FIG. 9.

of the left eye was noted in the inferior temporal sector of the disc. It was oval in shape, greenish-grey in colour and apparently quite deep, although the depth of the " pit " could not be ascertained both on account of the connective tissue overlay and the obliquity of extension of the hole. Two small vessels approached this crater and then dipped very abruptly over its edge to disappear into its depth. A rather pronounced physiological cup was present in this disc (Fig. 10).

CASE 6. This patient was a 47-year-old female who recently developed symptoms of presbyopia. She had never suffered from any eye condition. There were no irritative phenomena, headaches or blurred vision. Within the past six months difficulty in threading a needle and in reading telephone type had become more and more pronounced. The patient's vision was 20/25 in each eye and was readily corrected to 20/20 in each. The right pupil was smaller than the left. Although each pupil reacted to light and to accommodation, the response of the left pupil was not very prompt to light. There was considerable atrophy of the inner circle of the

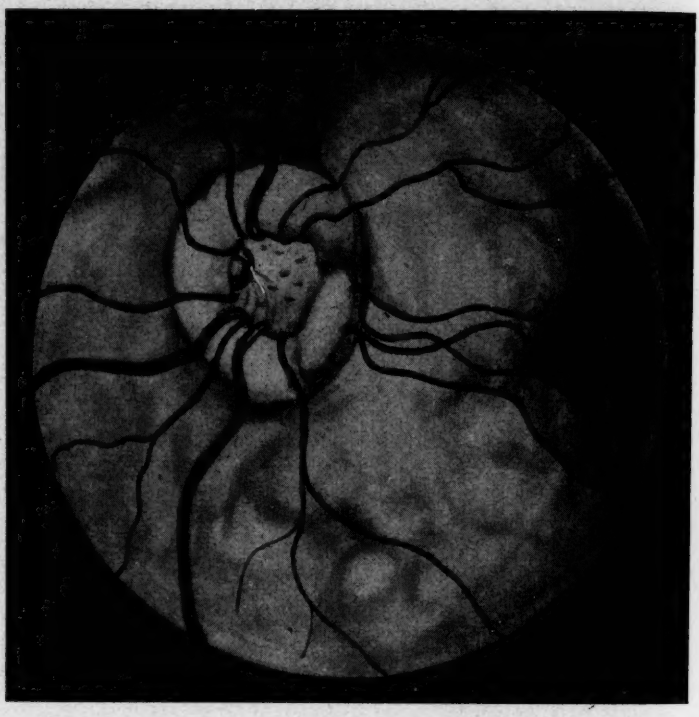


FIG. 10.

iris of the left eye with a very mild degree of iris atrophy on the right side. The media were clear. The fundus of the right eye appeared perfectly normal. The left fundus presented the anomaly shown in the fundus photograph (Fig. 11). The fundus in general was albinoid with the choroidal circulation readily showing through to the retina. The disc was slightly oval in shape with the upper four-fifths appearing quite normal in all respects but the lower fifth presented an anomalous depression. This lunar-shaped depression was five dioptres in depth, greyish-green in colour and covered by a thin irregularly-formed veil. On the temporal side two vessels disappeared suddenly just beyond the margin of the cup to become visible again in the depths of the depression. On the nasal side one large vein was seen dipping abruptly into the cup and reappearing just beyond the margin of the disc. The vessel pattern was not particularly abnormal. Because of the irregularity in the size of the pupil, the atrophy of

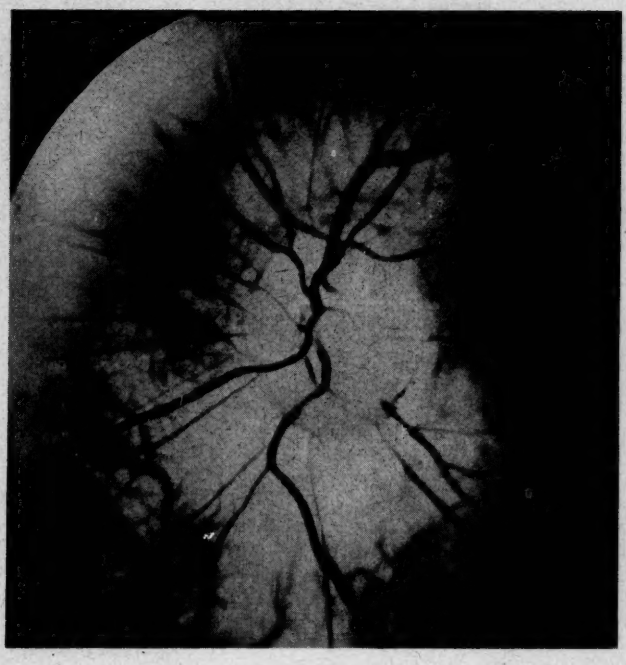


FIG. 11.

the iris, the appearance of the left disc and because of lack of familiarity of the condition of " pits " a study was made of the patient's intra-ocular pressure, but the diurnal curve failed to show any variation of significance. Provocative tests (*i.e.*, dark room, dilatation, coffee, excess of fluids), caused no increase in the intra-ocular pressure. Studies made upon visual fields and blind spots showed a defect associated with the congenital " pit " (Fig. 12).

CASE 7. This 42-year-old female first sought aid because of persistent diplopia, headaches, nausea and vomiting. For many years she had been able to read only if one eye was kept closed. She also noticed that the left lid had a tendency to droop, the condition becoming quite pronounced when she gazed into the mirror. The patient was found to have a paresis of the left superior rectus muscle along with a pseudoptosis. The fundus of the right eye appeared normal. The fundus of the left eye showed a peculiar cupping of the nerve head. In the lower outer quadrant there was a small partial coloboma about 1/8 D.D in size and slightly bluish

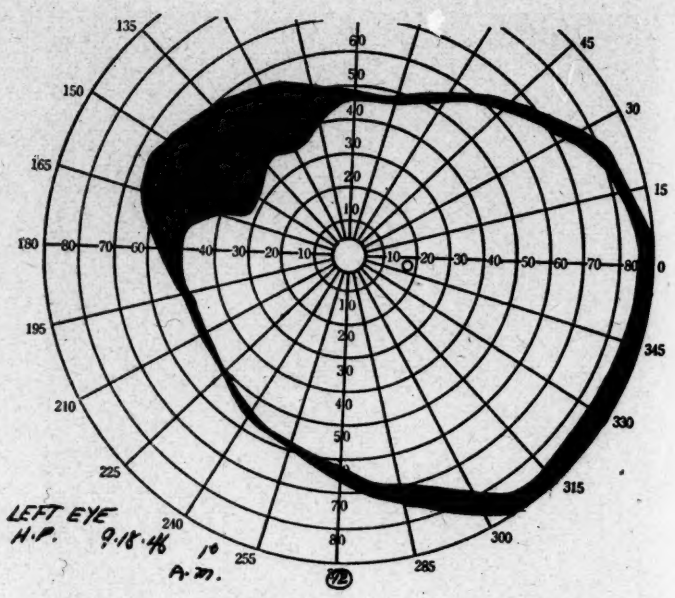


FIG. 12.

in colour. It was covered over by a connective tissue membrane so completely that no depth could be determined for the hole formation.

Discussion

Most case reports of this condition show the crater to be present in the temporal half of the disc and usually in the lower portion. The " pit " never extends beyond the edge of the disc although that structure may be distorted in a horizontal direction. A. Fuchs[2] stated that congenital " pits " occupy the sclera adjacent to the lower margin of the papilla and only exceptionally are they seated within the papilla itself. Fuchs presented a very rare case in which a congenital " pit " was within the excavation of a glaucomatous cup. Most " holes " appear to be directed backwards in a straight and not an oblique fashion. Cases 3 and 5 in our series appeared to be somewhat oblique. Also in Case 3 the temporal margin of the disc appeared to be unusually sharp. In three instances the depth of the " pit " could not be ascertained in our cases; in case I the " crater " was seven or eight dioptres in depth. In a case reported by Moffatt[4] it was noted that the darkest part of the

hole was at its outer edge giving the impression that the deepest portion of the "pit" was behind the overhanging edge of the sclera. This same appearance was also noticed in our third case. In a case reported by Neame[5] the patient noticed a gap in his visual field which caused him to seek aid much as occurred in our second case. Mann[6] states "there are no vessels in the pits," which statement is apparently not true, for in a case reported by Nielson[7] the author states that "vessels descended at the edge of the groove and reappeared upon the other side." Several of our cases also show vessels within the "pits."

A case presented by G. Edmund[8] showed a groove which occupied the entire temporal half of the disc and reached completely to its margin. This groove was darker in colour but only three dioptres in depth. A second case reported by this author showed an inferior conus with a horizontally oval hole lying between the disc and the crescent. This second case had iridodonesis which was pointed out as a factor in suggesting that the condition is one of congenital abnormality. Other anomalies are said to be associated with this condition—*i.e.*, microphthalmia, ectopia lentis, coloboma, persistent hyaloid artery, etc—but none was observed in our case reports.

Most authors believe the "holes" are colobomata. They may be the result of defective foetal cleft closure, or a remnant of the hollow which connects the optic cup with the cavity of the optic stalk. Wessely[9] believes the "pits" are remains through which have passed cilio-retinal or optico-ciliary vessels whose atrophy had been completed rather late in intra-uterine life. Edmund[8] thinks the "pits" are the results of abnormal vascular grooves. Alabaster[10] expressed the opinion that a vascular accident caused a collapse of the small capillaries in the nerve head with a defect subsequently remaining. Mann[6] states that in all probability these defects *are not holes*, believing that their nature is not always clear since they seldom come to microscopic examination. She furthermore states they may be cysts or pockets filled with transparent tissue, but there is no clinical evidence that these structures are cystic. Greear[2] has emphasized that the condition is not a true coloboma which would be secondary to disturbance of closure of the foetal fissure. He states that these "pits" are atypical colobomata by which is meant that the "pit" resembles a coloboma but has its origin in an entirely different manner.

SUMMARY. Crater-like holes may be erroneously regarded as evidence of glaucomatous changes, particularly when there are pupillary inequalities, iris atrophy and field defects. They may also be present in amblyopic eyes in which instance, recognition

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should lead to avoidance of occlusion therapy. The field defect may be quite constant and may be recognised by an observant patient. Case 4 would tend to strengthen the belief that the condition is a congenital one. The possibility of such a "pit" extending back into the orbit and uniting with a cyst, thus producing unilateral exophthalmos, should also be borne in mind[12].

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A CASE OF A GRÖNBLAD-STRANDBERG SYNDROME, WITH DISCIFORM DEGENERATION OF THE MACULAE*

BY

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IN March, 1946, C. R., male, married, aged 38 years, a motor salesman, noticed distortion of objects to his right side, most noticeable when he was car driving, and absent when he closed his right eye. At that time, his visual acuity was 6/5 6/5 (Snellen) with no error of refraction and at six metres, there was Δ 1/4 left hyperphoria, and at 20 cms. esophoria 3°. The media were clear, but each fundus showed several, small, scattered, ovoid patches of yellow-white exudate with discrete, faintly pigmented margins, two of which were in the right macular area. Over these, the macular capillaries were without distortion or interruption.

During one year, the case was repeatedly examined, and several, new, small patches of exudate were seen to form in the mid-periphery of each eye.

In March, 1947, several new patches were seen in the right

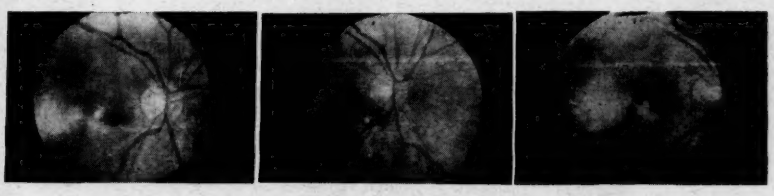
* Received for publication, March 11, 1948.

macular area, and subjective testing on Bjerrum screen at two metres revealed a scotoma in the right central area of the field of vision, with a dense nucleus and sloping edge which overlapped the fixation point. The vision of this eye was reduced to 6/24 by April, 1947.

The case was observed closely, and in September, 1947, the patient reported rapid failure of central vision for all purposes, including close work during one week. He was unable to read newsprint, and objects seen with the left eye appeared distorted and blurred. Visual acuity was then O.D. less than 6/60; O.S. 6/36 partly.

The scotoma, recorded before as present in the right central area, was found on Bjerrum screen at two metres, to be more extensive, with a larger, dense nucleus and steeper margins. The scotoma was dense to targets of less size than 10/2000 white (artificial light 100 watt 6 feet above patient). The left field of vision showed a small, central scotoma, relative in quality.

The right fundus, at this time, showed a roughly circular, white patch of exudate in the macular area, approximately twice the size of the optic disc, over which the macular capillaries ran without distortion, though standing out well against the brilliant white background of exudate. This patch gave the impression of being slightly raised above the level of the surrounding normal retina. To the nasal side of the disc, a brown-black angeoid streak was



PHOTOGRAPHS 1-3.

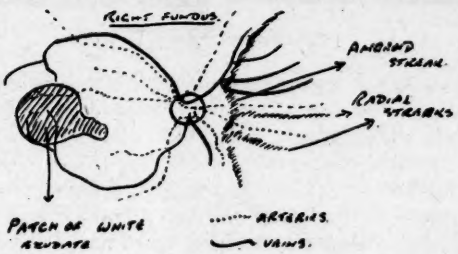


DIAGRAM 1.

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present with indistinct powdery margins, equal in width to an artery of first division of the central retinal artery, and curved concentrically with the disc margin, separated from this by a narrow interval. Three angeoid streaks ran radially from the convex border of this out towards the nasal mid-periphery of the fundus. (See photographs 1-3 and diagram 1.)

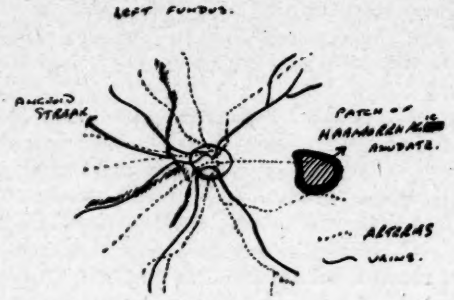
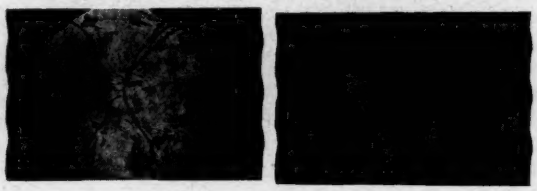


DIAGRAM 2.

The left fundus showed a "haemorrhagic" patch of exudate, roughly circular, in the macular area, and one half the size of the optic disc. This patch increased in size from day to day, becoming constant at the side seen in photographs 4-5 and acquiring a grey-black centre and brown-black margin, as is well seen in the photographs as two separate densities.



PHOTOGRAPHS 4-5.

An angeoid streak was present in the left eye, similar in appearance to that in the right fundus, but placed nearer to the disc margin on its nasal side.

On each fundus, the retinal vessels were normal in appearance, while the patches of exudate in the mid periphery of each fundus were not related to the radial angeoid streaks. The retinal vessels crossed the angeoid streaks without deformation or distortion.

Throughout the period of observation, no signs of uveitis have

appeared, with absence of " K.P." aqueous or vitreous haze, and ciliary injection, while the fields of vision remained of normal, relative extent.

A discrete patch of pigmentation on the anterior surface of the right iris has remained unaltered.

During the period of observation, it was noticed that the patient had altered skin of the left side of the neck. Similar changes were found on extensive areas over the epigastrium, lower chest anteriorly, the anterior fold of the left axilla, and the skin of each antecubital fossa and axilla. In all these areas, the skin was soft, thin when picked up between finger and thumb, excessively mobile on the underlying tissues, and possessed a fine mosaic of yellow ridges, less than a millimetre in width, easily palpable to the pulp of the examining middle finger. The effect of voluntary contraction of platysma myoides on the skin of the neck was less on the left side than on the right. One café-au-lait stain, the size of a British penny postage stamp, was present over the left temporal region.

Investigations

March, 1946.

	$\frac{1}{1,000}$	negative
Mantoux intradermal skin test	$\frac{1}{10,000}$	negative
	$\frac{1}{100,000}$	negative

Wassermann (venous blood), negative. B.P. 160/70. Chest X-ray.—No abnormality seen. X-ray teeth.—Apical infection of two teeth. These were extracted.

September, 1947.

X-ray paranasal sinuses.—" Loculated type of antrum on the right side, with diminished translucency of part of the antrum. ? Congenital anomaly ? after infection." There are no clinical signs or symptoms of antrum disease.

October, 1947.

X-ray skull and pelvis.—" There is no evidence of Paget's disease of bone."

B.S.R. 3mm. in one hour. Coagulation time, 2 mins. 40 secs. Bleeding time, 7 mins. 30 secs. Hb. 92 per cent. R.B.C.'s, 5·06 million. C.I. 0·92. W.B.C.'s 12,600. Polymorphs 62 per cent. Eosinophils 1 per cent. Basoph 1 per cent. Lymphocytes 30 per cent. Mononuclears 6 per cent. The red cells were of normal shape, size and staining. Capillary fragility test.—Slight increase.

Urine.—No abnormal constituents.

V.—O.D. less than 6/60. O.S. 6/60, with −0·50 D.Sph. added—part of 6/36; eccentric fixation—part of 6/24.

The patient readily and suddenly learned to appreciate the value of fixing slightly to one side of the object of regard.

Telescopic lens systems. (Hamblin's). O.D. 6/60. O.S. 6/36 with −1·00 D.Sph. placed behind the system.

part of $\frac{6/24 \text{ direct fixation.}}{6/18 \text{ eccentric fixation.}}$

With a 12 D.Sph. small lens added to the system. O.D. J.16 read badly. O.S. J. 10 read rapidly and well.

General physical examination showed no abnormal signs, radial pulses equal and normal, 72 per min. There is no history and no other sign of peripheral vascular disease except a history of pain in both calves after walking about a mile or so. This pain subsides after resting, but is inconstant in incidence.

Family History.—The father and mother died aged 75 years and 77 years respectively, and one brother died as a youth of tuberculous peritonitis.

One sister has normal vision, and the patient knows of three cousins with no history of eye disease, though none was available for examination.

Diagnosis.—When the case was first seen, the diagnosis was disseminated choroiditis, using the term in a descriptive sense, rather than the narrower sense of implying the common picture of syphilitic choroiditis.

The significance of the angeoid streaks was clearly recognised and a bad prognosis given.

The skin condition was not discovered until September, 1947. The patient gives a long history of unusual skin texture in the areas described, with no recent change.

The changes in each macular area have been labelled disciform degeneration, and the photographs show perhaps two stages in a common process, the right eye a late stage, the left an early "haemorrhagic" state.

Treatment.—Focal sepsis was searched for, but, apart from the teeth mentioned, none was found.

Sulpha drug, penicillin, mixed vitamins, iodides, salicylates, coagulin ciba, and other drugs have been given a trial, but the case has steadily progressed to the present state.

Photographs and diagrams

Comments on Photographs.—These photographs stress the severe limitation of fundus photography as so far evolved. In them, the size of the areas of macular exudate is shown, and

the difference in appearance on the two sides is also shown well. The angeoid streaks are recorded but faintly and appear similar in the one side on photographs 1 and 2—as opposed to obvious defects and artefacts which have moved in position on the two photographs.

The arteries and veins of the same fundus differ in different photographs in apparent diameter and appearance. This illustrates my personal opinion that fundus photography cannot be held to record accurately such factors as the nature of the light streak, arterio-venous crossings, venal diameter, though the degree of tortuosity (or " straightness "), especially of macular capillaries, can be recorded thus.

This opinion I have reached after photographing a series of 150 fundi in healthy persons of greater age than forty years.

The Grönblad-Strandberg syndrome consists of angioid streaks of the fundi with pseudo-xanthoma of the skin. Originally described by Grönblad, with Strandberg as the authority on the skin condition, this syndrome has been repeatedly found and cases published.

The existence of other abnormalities has been found in the presence of the syndrome, or of the angeoid streaks.

The syndrome, plus exudation at the macula resembling disciform degeneration, was described by Goedbloed[2] who quotes Wildi, 1926, as describing three stages of development of the lesion in the macular area.

1. Streaks with normal central fundus.
2. Detachment of the retina by exudate in the macular area.
3. Organisation of the exudate to form a grey disc.

The case described falls broadly into this description.

Angeoid streaks and senile elastosis of the skin are associated in two cases by Goedbloed[2].

Angeoid streaks and Paget's osteitis deformans of bone have been described by Terry[3], Lambert[4] and others[8]. The syndrome, however, has not been described in the presence of Paget's disease.

A case of moderately advanced Paget's disease was observed by me over a period of twelve months, and developed scattered small areas of yellow exudate in both fundi, some in the central areas. There were no skin changes in this case, and no streaks. The familial tendancy of streaks has been established by Law[9], Wassenaar[10], Goedbloed[2], who quotes Franceschetti, and Roulet, 1936, and the factor appears to be recessive.

Pathological studies by Hagedoorn[5] suggested degeneration of elastic tissue of Bruch's membrane, with perhaps similar alteration of the elastic structure of blood vessels. Law[9] found folding of the

retina and accumulation of pigmented débris to coincide with the streaks.

Recently, attention has been given to the blood vessels of the extremities in cases of angeoid streaks by Guenther[6] and Scheie[7] with Freeman[7]. Guenther investigated pulse wave velocity and form in the peripheral musculo-elastic arteries (Muskelelastische Arterien) in nine cases of the syndrome, eight of arteriosclerosis, and nineteen " normals." The velocity was lower in the syndrome cases, while the proportion of the height of the base of the incisure, compared with the amplitude, expressed as a percentage, was higher than normal.

The alterations found were considered significant, and indicative of degeneration of the elastic tissue elements of the vessel walls. There was no confirmation by biopsy of the vessels. Symptoms attributed to vascular changes were weakness of extremities, coldness of hands and feet, dyspnoea. Scheie[7] and Freeman[7] supply some confirmation in describing three cases of streaks. In two cases, the whole syndrome was present, with severe vascular disturbances in the limbs. Absence or diminution of pulsation of peripheral arteries was present. Oscillometric records of pulsation showed a generally diminished amplitude in these vessels in both cases. In one case, biopsy of an ulnar artery was carried out. The diminished pulsations were confirmed during the dissection.

Histologically, the intima and internal elastic lamina were normal. The media showed fragmentation and vacuolation of elastic tissue by Weigert's stain to a marked degree. There was hypertrophy of muscle fibres.

In both cases showing vascular abnormalities, calcification of major limb vessels was evident radiographically. These writers suggest routine ophthalmoscopic examination of cases of unexplained peripheral vascular disease.

The association of Paget's disease with the angeoid streaks, angeoid streaks with changes in the dermal elastic tissue, the streaks and skin changes with peripheral vascular disease, and with abnormal calcification of peripheral major vessels, point to a probable common factor. Perhaps more systematic investigation of each type of case may be productive of further knowledge, but the tendency for each writer to be confined to a small collection of each manifestation operates against this.

Permission to publish the account of this case by Mr. J. J. McCann, F.R.C.S., of Liverpool, under whose care the case was observed, is acknowledged. Use of the fundus camera at the Liverpool Medical Research Institute was granted by the Director, Dr. I. Harris, Liverpool.

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A MYXO-HAEMANGIOMA SIMPLEX OF THE CONJUNCTIVA BULBI*

BY

A. BAKKER

GRONINGEN

A WOMAN, aged 35 years, came into my consulting-room, complaining that she had the sensation of a foreign body in her right eye. For six weeks she was aware of the presence of a small tumour in the inner angle. Nothing was known about any trauma. The tumour was growing rapidly and at the time of my investigation it was about 4 mm. high and had a diameter of 3 mm. It was of a fungus like shape and had a broad and short pedicle. It was movable on the underlying tissue. Its base was partly covered by the semilunar plica. The tumour had a cherry-red colour and a smooth surface. At its base a tortuous and dilated vessel was visible.

Because of its disfiguring effect and its rapid growth I decided to remove the tumour. This was performed under cocaine anaesthesia. The tumour was excised by the single snip of a pair of scissors. There was little or no haemorrhage. Fixation with Bouin's liquid.

The microscopical examination gave the following picture: The whole tumour is completely covered with normal epithelium, containing many goblet cells (Fig. 1). The main substance of the tumour consists of compactly arranged small blood-vessels (dilated capillaries). The endothelial cells are extremely swollen. Here and there we find more than one layer, so that the lumen is obliterated by them. Some larger vessels intersect the tumour. In various sections we see large oedematous areas and some smaller

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FIG. 1.

interstitial haemorrhages, probably the result of interference with the blood circulation. The anatomical substrate of the impairment of the normal blood supply we see in the thrombotic vessels in the tissue subjacent to the tumour (episclera). At the same time these clotted vessels give us the explanation of the fact that the excision of the tumour caused practically no haemorrhage. The tumour is surrounded by a thin fibrous capsule. The connective tissue in the tumour is very poorly developed. In the sections, stained after Mallory, we see only an extremely delicate network of blue fibres round the capillaries. At many places several free macrophages are visible. They are loaded with pigment granules, being the result of incorporated red blood-corpuscles. Also some plasma-cells are present. At the base of the neoplasm, outside the capsule, we notice a lymphocytic infiltration under the epithelium. At the periphery of the tumour, but inside its capsule, we see a large jelly-like, oedematous area with a great number of spindle-shaped cells, which constitute a wide-meshed network. Most of these cells are unmistakably sprouting endothelial cells, but among them we also find young fibroblasts, which give rise to the formation of a meshwork of delicate connective tissue fibres. The homogeneous substance lying in the meshes gives a positive mucin-reaction with thionin. It is this area where the tumour obviously shows signs of an intensive growth, but also the mitotic figures in the depth of the tumour give evidence of a constant proliferation. With these symptoms the rapid growth of the neoplasm is fully explained.

FIG. 2.

In Figure 2 we see under a higher magnifying power a tangentially cut section of the tumour, just outside the pedicle. The above-described reticular tissue, consisting of young fibroblasts and proliferating endothelium-cells, can be distinctly seen.

Coming to the point of making a diagnosis, we may say that in the underlying case we have to do with a haemangioma simplex of the conjunctiva bulbi, which simultaneously shows signs of an intensive proliferation and a myxomatous degeneration.

Discussion

Pedunculated haemangiomata of the conjunctiva bulbi are very seldom described in the ophthalmological literature. This is the reason that I thought it worth while to publish this case.

Among a great number of polypoid tumours of the conjunctiva which Elschnig[1] collected from the literature, he did not find typical angiomata with certainty. In a survey Pergens[2] reviews 52 cases of conjunctival haemangiomata (including two of his own). The majority of the tumours of the conjunctiva bulbi were situated in the inner angle of the eye. None of them resembled the neoplasm of my case. James and Trevor[3] report on two cases of haemangioma simplex arising from the palpebral conjunctiva. Their second case perhaps resembles somewhat the tumour in my case, but there is certainly a striking difference in the amount of connective tissue, which was in my case practically absent, so that the capillaries with their swollen endothelial cells were lying almost immediately next each other. Pendleton White[4] gives a description

of a capillary angioma arising from the palpebral conjunctiva of the upper eyelid. Here the convoluted thin-walled vessels were embedded in great masses of lymphocytes.

Maxted[5] describes a pedunculated angioma of the conjunctiva of the upper eyelid, which perhaps shows some resemblance to my case.

Summarizing we can say that a tumour similar to the fungus-like haemangioma of the conjunctiva bulbi in my case, has not been previously described. The fact that symptoms of intensive growth synchronised with myxomatous degeneration is noteworthy.

After eight months no recurrence has followed.

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THE PROGNOSIS OF RETROBULBAR NEURITIS*

BY

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VARIOUS theories as to the aetiological factors concerned in the production of retrobulbar neuritis have been postulated from time to time. In the days prior to the Wassermann reaction, a large number of cases were considered to be syphilitic in origin, and further evidence for this aetiology was given by a good response to mercury therapy. We now know that most cases of retrobulbar neuritis clear up rapidly without treatment. English authors have regarded disseminated sclerosis as the commonest cause of retrobulbar neuritis: Buzzard (1930) quotes Gowers as saying that gout is the next most frequent cause after disseminated sclerosis.

Marcus Gunn (1904) listed the following as possible causes in a series of 380 cases (tobacco amblyopia being excluded):—Periostitis 40, exposure to cold 27, dental sepsis 17, nasal sepsis 42, gumma 16, disseminated sclerosis 51, influenza 27, gout 22, varied (ptomaine poisoning, malaria, and constipation) 63, obscure 58, and the proportion of men to women was in the ratio of 31:27.

Marchesani (1936) in Bumke-Foerster's Handbuch der Neurologie lists the following figures: tumour (anterior fossa) 6, toxic 15, lactation 2, nasal sepsis 9, lues 24, disseminated sclerosis 113,

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encephalitis 7, meningitis 3, subacute combined degeneration 1, haematomyelia 1, vascular 4, tower skull 2, trauma 4, melaena 1, Mikulicz' syndrome 1, tenonitis 1, obscure 89.

Various factors have been definitely shown to produce retrobulbar neuritis other than those already mentioned. Amongst these must be included that of Cone (1938) and phenylaniline hair dyes described by Keschner and Rosen (1941).

Disease of the nasal passage and sinuses has been regarded as a potent cause of retrobulbar neuritis and operations on the sinuses were frequently advised. However, Traquair (1930) thought that all cases of idiopathic retrobulbar neuritis were probably due to disseminated sclerosis and that operation on the sinuses should not be performed. Chambers (1947), too, states that a series of cases of retrobulbar neuritis which he and Foster Moore examined showed no difference in prognosis whether the sinuses were operated on or not. Most neurologists now consider that disseminated sclerosis is the commonest cause of retrobulbar neuritis.

The incidence of a previous blindness in one or both eyes in patients with multiple sclerosis has varied according to the author concerned: Behr (1924) gives 75 per cent., Adie (1930) 30 per cent., Benedict (1942) 15 per cent. and Lillie (1934) 15 per cent. The percentage of cases of retrobulbar neuritis showing evidence of disseminated lesions at the time of blindness was 34 per cent. in a series of 34 cases recorded by Adie (1932).

Few cases have been followed up over a long period to ascertain how many later developed neurological lesions elsewhere. Bruns-Stolting (1900), Fleischer (1908), Langenbeck (1914), Marburg (1920) all state that varying percentages of patients with retrobulbar neuritis " later " developed abnormal neurological signs indicative of disseminated sclerosis; Fleischer (1908) gives 21 out of 30; Marburg (1920) 14 out of 24; Langenbeck (1914) 33 1/3 per cent.; Behr (1924) states that 70 per cent. " later " developed abnormal neurological signs compatible with disseminated sclerosis; Weill (1923) states that of 23 cases examined, 11 already had disseminated sclerosis and that a further five had developed it " some " years later; Friedinger (1925) followed up 25 cases from five to twenty years, 16 of these being followed for 11 years and two had by that time developed disseminated sclerosis—one other case was found in the other nine cases followed up for 20 years. Lactation optic neuritis described by Langenbeck (1914) and Schöppe (1919) was regarded as probably disseminated sclerosis by the former author, for a third of his cases were later found to develop this disease. Hensen (1924) states that a persisting scotoma is later associated with abnormal neurological signs.

Lenoir (1917), on the other hand, states that practically no cases developed signs indicative of a disseminated lesion. The literature on the subject is therefore conflicting, few cases having been followed for any length of time; this article is therefore concerned with the ultimate prognosis of retrobulbar neuritis followed up for over ten years.

Investigation

The out-patients record of the Bristol Eye Hospital from 1933 to 1937 were searched for patients diagnosed as suffering from retrobulbar neuritis. Included in this unselected series are cases due to all causes except syphilis, and to them are added patients attending the in-patient department as far back as 1902. Cases were diagnosed on suddenness of onset of visual failure, papillitis in some cases and usually recovery of vision through a central scotoma. Only forty-six patients so diagnosed were found; eleven of these could not be traced due to changes in address and bombing in the war years, but four deaths which were traced are included in the remaining thirty-five of the series.

Age of onset

The age of onset varied from 14 to 63 years; in the untraced series the average age was 30 years and in the traced 27 years; the ratio of female to male was six to five in the untraced and nineteen to sixteen in the traced. There appeared to be no significant difference in the age of onset as regards sex in either series.

Deaths

Four deaths were found in the series studied; one patient was killed in an accident and two died of natural causes; in none of these could death be connected with a demyelinating process. It is of particular interest that one patient who had a bilateral retrobulbar neuritis and had a negative blood Wassermann, but in whom no cerebrospinal fluid examination was made, died of general paralysis of the insane in a mental institution eight years later; it therefore appears that examination of the cerebro-spinal fluid should be carried out in cases of retrobulbar neuritis.

Relation to pregnancy

Out of ten women examined who had had children, only two related their onset of symptoms of eye trouble to pregnancy, but one woman had later developed an acute disseminated lesion following a further pregnancy (Case 14).

Occupation

No special incidence of any occupation was found; one patient out of the traced series had worked as a pottery glazer and he was the only one who was definitely exposed to lead.

The left eye was affected in twenty-three cases, and the right in thirteen; ten patients had bilateral involvement. Six of the latter were examined; two were found to be blind in both eyes (Cases 4 and 29), two had made a complete recovery in one eye and two had made a complete recovery in both eyes. Of the other twenty-four traced cases only one was found to be blind in the affected eye. Indeed, most patients made a complete recovery in visual acuity of the previously affected eye; the ultimate prognosis of visual acuity appears therefore to be quite favourable.

Incidence of nervous disease in relatives

In one case only was there a familial incidence of a nervous disease (Case No. 13). This patient's sister had died three years previously to the patient's onset of retrobulbar neuritis; her hospital record notes showed that she was admitted for investigation of blindness and a "Parkinsonlike" tremor associated with bilateral extensor responses at the age of seventeen, and that she died six months later at home, no post-mortem being performed.

Fundus

Examination of the fundus showed varying degrees of optic atrophy in the eye previously affected by optic neuritis.

Abnormal neurological findings at the onset of ocular neuritis

Available records showed that four out of the thirty-six traced cases had abnormal findings when examined by a neurologist at the time of onset of retrobulbar neuritis; these four cases (Nos. 24, 28, 8 and 11) will now be described briefly.

CASE 24.—Fourteen years previously, when aged sixty-three years, the patient had developed an acute pain in the left eye with vision reduced to $\frac{1}{2}/60$ and a central scotoma present on examination of the fields. At that time he had a left extensor response, but no other abnormal neurological signs; examination of the cerebrospinal fluid showed normal protein, Lange curve and cells with a negative Wassermann. On examination at follow-up, the patient's acuity was now 6/6, the left optic disc was pale and the left plantar response was still extensor; there were no other abnormal neurological findings nor had the patient had any abnormal subjective feelings in the interim period.

CASE 28.—Twelve years previously, when aged fourteen years, the patient's vision had failed suddenly with reduction of acuity to 1/60 in both eyes. X-rays of skull and sinuses were normal; blood and cerebro-spinal fluid Wassermann were all negative, and examination of the central nervous system showed the presence of bilateral extensor responses. When examined at a follow-up the patient felt quite fit and had served throughout the 1939-45 War in the Pioneer Corps. His visual acuity was now limited to perception of finger movements in the right eye, and 6/36 in the left; examination of the fundi showed a bilateral optic atrophy more advanced in the right than in the left. The rest of the central nervous system was normal except for a right extensor response. He, too, had no subjective evidence of any abnormal neurological disorder.

CASE 8.—This patient, an agricultural labourer, developed an acute failure of vision seventeen years ago when aged thirty-two years; at that time he had bilateral blurring of the optic discs with acuity reduced to 4/60 in the left and 6/36 in the right, the cerebro-spinal fluid examination was normal in all respects, except for the Lange curve of 12222100; his plantar responses were extensor. When examined at follow-up, he had a bilateral optic pallor, visual acuity 6/9 right and left, and no abnormal neurological signs except for bilateral extensor responses. He felt well and was actively employed as a farm tractor driver.

CASE 11.—This patient developed a sudden blindness of the right eye twenty years ago when aged eighteen years. At that time she had a papillitis of the right optic nerve and bilateral extensor responses. Since then she had gradually developed further neurological lesions year after year, with intermissions and exacerbations. On follow-up examination she was bed-ridden, with bilateral optic atrophy, nystagmus in all directions, paresis of the left sixth cranial nerve and a gross inco-ordination of arms and legs. She had a severe degree of impairment of joint sensibility, worse in the legs than the arms, and a spastic quadriplegia with bilateral extensor responses completed a depressing picture.

The presence of abnormal neurological findings in a patient with a retrobulbar neuritis does not necessarily indicate a bad prognosis, as the above case records show that some patients lead full and active lives for many years afterwards.

Incidence of further abnormal neurological findings compatible with the diagnosis of a demyelinating disease

Abnormal neurological findings were present in twelve of the thirty patients examined: six of these could be definitely diagnosed as suffering from disseminated sclerosis, and six probably affected

TABLE I

Years followed up	Number of cases	Number with definite Disseminated (Case series numbers in brackets)	Number with probable Disseminated (Case series numbers in brackets)	Number with no evidence of Disseminated (Case series numbers in brackets)
10	1	0	0	1 (20)
11	2	0	0	2 (12.31†)
12	4	2 (2.3)	1 (28*)	1 (30)
13	7	0	1 (6)	6 (10.15.16.17.18.25)
14	10	3 (5.14.21)	1 (24*)	6 (1.9.12.22.26.27)
17	1	0	1 (8*)	0
19	1	0	0	1 (23)
20	2	1 (11*)	1 (7)	0
45	2	0	1 (4)	1 (29)
47	1	0	0	1 (19)
Total	31	6	6	19

* = Had abnormal neurological findings at onset of retrobulbar neuritis.
† = Refused to be examined.

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by this disease. The findings varied greatly, some had numbness of both legs, others transient numbness of leg or arm, and others said they were quite well but on examination abnormal plantar responses were found. One only of the whole series (Case 11) was confined to bed, all the rest were in fact leading useful and productive lives, for the two blind patients were employed at basket making.

Discussion and Summary

The purpose of this paper was to discover how many patients with retrobulbar neuritis eventually developed disseminated sclerosis after a number of years. Only five patients answered a written questionnaire by post, stating that they had nervous diseases, but in fact twelve out of thirty cases actually examined showed evidence of abnormal neurological findings. The incidence of previous organic disease amongst the population is therefore probably much higher than is usually realised, for only three of these twelve patients were under medical supervision and only one of these was bed-ridden. This may indicate that the occurrence of disseminated sclerosis is higher than previous figures have shown.

The prognosis for visual recovery appears to be excellent on the whole, only one out of the twenty-five unilateral cases being blind in the affected eye a considerable number of years after. The prognosis with regard to further demyelination elsewhere in the central nervous system is more difficult to estimate; in fact it is impossible to give a prognosis in these cases, as one patient with a bilateral retrobulbar neuritis was in excellent health forty-seven years later. In addition, it has been shown in this survey that the presence of abnormal neurological findings at the onset of retrobulbar neuritis does not necessarily mean a bad prognosis.

The eleven patients who were untraced might conceivably have died of disseminated sclerosis, but it is suggested that migration of population during the war years had a great deal to do with the fact that they were untraceable. In fact, three of these were domestic servants and one was an inmate at a Salvation Army Hostel.

Finally, the importance of doing not only blood Wassermann reactions on these patients but full cerebro-spinal fluid examinations to exclude syphilis is stressed in this paper. One patient in whom this was neglected was later found to have developed cerebral syphilis.

Conclusions

1. Forty-six cases of retrobulbar neuritis were taken from hospital records. Eleven were not traced, four were dead and one

refused examination. The thirty cases left were examined from ten to forty-seven years later.

2. Twelve patients were found to have abnormal neurological signs apart from the eyes, but only one was bed-ridden with disseminated sclerosis.

3. The eventual prognosis of visual recovery was good. Of the twenty-four unilateral cases, one was blind; and of the six bilateral cases two were blind in both eyes and two blind in one eye.

4. The importance of examination of cerebro-spinal fluid for evidence of syphilis in cases of retrobulbar neuritis is stressed.

I wish to thank Dr. A. M. G. Campbell for his continued interest and help in the compilation of this work, and the Honorary Staff of the Bristol Eye Hospital for allowing me to see their case notes.

Case histories

A. DEFINITE DIAGNOSIS OF DISSEMINATED SCLEROSIS.

CASE 2. Female. Sudden onset of painful blindness of left eye with papillitis twelve years ago when aged twenty-one. Seven years ago the patient developed transient numbness below the umbilicus, which recovered; since then had further attacks of numbness. On examination there was loss of vibration sense and joint sense in the left arm and right leg. The diagnosis of disseminated sclerosis had been confirmed by Professor Cloake, of Birmingham.

CASE 3. Female. Sudden onset of painful blindness in right eye twelve years ago, when aged twenty-six. Complete recovery of vision in a month followed by a recurrence in the same eye nine years later with an associated numbness up to the middle of the waist. Examination now showed loss of vibration sense in the left leg with bilateral extensor responses.

CASE 5. Female. Sudden onset of loss of vision in the left eye when aged twenty-seven, fourteen years ago. Recurrent ataxic episodes since, transient numbness in face and left arm with peripheral numbness recently. Diagnosed as disseminated sclerosis by Dr. Russell Brain.

CASE 14. Female. Sudden failure of right vision fourteen years ago, when aged twenty-one. The patient had been quite well till nine months prior to examination when, following a pregnancy, she developed subjective numbness from the umbilicus downwards. Physical examination revealed a sensory loss below the level of the eighth thoracic dermatome, and a spastic paraplegia with bilateral extensor responses.

CASE 21. Female. Sudden onset of failure of left vision fourteen years ago, when aged twenty-two. The patient stated she felt quite well, but physical examination showed ataxia and diminished vibration sense in the left leg, with bilateral extensor responses.

B. PROBABLE DIAGNOSIS OF DISSEMINATED SCLEROSIS.

CASE 4. Male. Sudden failure of vision of the right eye forty-five years previously, when aged sixteen. This recovered after a few months, but two years later he developed a visual failure of the left eye; this too recovered. At the age of thirty-three the patient developed blindness in his right eye from which he never recovered, and at forty-two he developed a blindness of the left eye. On examination at the age of sixty-three, the patient was completely blind in both eyes with a bilateral optic atrophy; he had bilateral extensor responses but made

no complaint of any ill-health at all and was actively employed at basket-making.

CASE 6. Male. Sudden onset of painful visual failure in left eye when aged thirty-five, twelve years ago. Complete recovery of visual acuity. Patient stated he felt quite well (a patient in Ham Green Sanatorium for pulmonary tuberculosis), but bilateral extensor responses were found on examination.

CASE 7. Female. Sudden onset of failure of vision in the right eye twenty years ago, when aged twenty-three. Patient had developed numbness in the right leg 14 days prior to examination; this was confirmed by sensory testing, and there was found to be a right extensor response.

C. NO EVIDENCE OF DISSEMINATED SCLEROSIS.

CASE 1. Male. Sudden onset of painful blindness of left eye with papillitis fourteen years ago, when aged twenty-five. No abnormal neurological signs now.

CASE 9. Male. Sudden onset of visual failure in the left eye fourteen years ago, when aged twenty-two. No abnormal neurological findings now, and no subjective symptoms.

CASE 10. Male. Sudden onset of right visual failure associated with pain fourteen years ago, when aged twenty-one. No abnormal neurological findings now, and no subjective symptoms.

CASE 12. Male. Sudden onset of left visual failure eleven years ago, when aged thirty-six. Since then there have been no symptoms of neurological disease.

CASE 13. Female. Sudden failure of left vision fourteen years ago, when aged twenty-three. Since then there have been no symptoms of neurological disease.

CASE 15. Female. Sudden failure of left vision thirteen years ago, when aged thirty-four. Since then there have been no symptoms of neurological disease.

CASE 16. Female. Sudden failure of left vision thirteen years ago, when aged fifty-two. Since then there have been no symptoms of neurological disease.

CASE 17. Female. Sudden failure of left vision thirteen years ago, when aged twenty-two. Since then there have been no symptoms of neurological disease.

CASE 18. Male. Sudden failure of right vision thirteen years ago, when aged twenty-one. Since then there have been no symptoms of neurological disease.

CASE 19. Female. Gradual failure in vision in both eyes in a few days without pain associated with a bilateral papillitis forty-seven years ago when aged twenty-one years. Visual acuity in the left eye 6/12, but hand movements only are perceived in the right eye. Since then there have been no symptoms of neurological disease.

CASE 20. Male. Sudden onset of visual failure ten years ago, when aged forty years. Since then there have been no symptoms of neurological disease.

CASE 22. Female. Sudden onset of left visual failure fourteen years ago, when aged thirty-two. Since then there have been no symptoms of neurological disease.

CASE 23. Female. Sudden onset of left visual failure nineteen years ago, when aged twenty-eight. Since then there have been no symptoms of neurological disease.

CASE 25. Female. Sudden onset of bilateral painful failure of vision with papillitis thirteen years ago, when aged twenty-four. Visual acuity now 6/6 right and left. Since then there have been no symptoms of neurological disease.

CASE 26. Female. Sudden onset of left visual failure when aged thirty-eight years, fourteen years ago. Since then there have been no symptoms of neurological disease.

CASE 27. Male. Sudden onset of left visual failure when aged eighteen years, fourteen years ago. Since then there have been no symptoms of neurological disease.

CASE 29. Female. Sudden bilateral failure of vision forty-five years ago, when aged seventeen. Partial recovery for nine months afterwards, and then a relapse into complete and total blindness. Examination showed a bilateral primary optic atrophy but no subjective or objective evidence of disseminated sclerosis.

CASE 30. Male. Sudden onset of right visual failure eleven years ago, when

aged twenty-nine. Since then there have been no symptoms of neurological disease.

CASE 31. Female. Sudden onset of left visual failure eleven years ago, when aged twenty-six. Patient refused to be examined and said she was quite well.

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TREATMENT OF SEVERE INFECTED CORNEAL ULCERS BY SUBCONJUNCTIVAL INJECTIONS OF PENICILLIN TWICE DAILY WITHOUT HOSPITALIZATION, WITH SHORT REVIEW OF OTHER METHODS*

BY

KAMEL RIZK

EL-MINIA, UPPER EGYPT

OCULISTS, like myself, who work alone in their clinics without medical assistants, look for a method of penicillin administration, which is practical, efficient and economic for the successful treatment of infected corneal ulcers. By the word "practical" I mean that it should not cause much strain either to the doctor or to the patient, or to his attendants at home, and should not interfere with their sleep. By the word "efficient" I mean that it should be able to control the infection instantly so that it spreads no more, and this control must be followed by rapid improvement and progressive healing. By the word "economic" I mean that the method should

* Received for publication, March 9, 1948.

not imply the use of much penicillin, as some patients are unable to pay the cost of penicillin if massive doses are to be used daily for few days. This point assumes special importance when we notice that severe infected ulcers of the cornea in Egypt mostly occur in the poorer classes who do not seek for medical advice except when their condition is very bad.

A brief review of the chief methods used is necessary, and we have to consider them in the light of the three criteria mentioned above.

One of the methods of penicillin administration for ocular affections is the systemic mode of administration used for a great variety of infections in general medical practice. Penicillin need not be administered intra-muscularly in aqueous solution or saline every three hours as this is not practical, but it can be given in massive doses suspended in oil and beeswax twice daily.

Sorsby and Ungar (1946*a*) showed that penicillin administered systemically in massive doses reaches in therapeutic levels all the tissues of the globe, the lens excepted. By massive doses is meant the injection of 25,000 to 50,000 units intra-muscularly or intra-venously into rabbits of an average weight of 1·5 kilograms. Duke-Elder (1947) commenting on this fact says that this dose is of the order of 40 or 50 times that of the usual clinical dose in man. We can imagine that massive doses administered systemically for ocular purposes must be very expensive apart from the other disadvantages such as difficulty of administration.

Local therapy by subconjunctival injections is much more economic than massive therapy by systemic administration. It may be noted that whenever subconjunctival injections of penicillin are mentioned in this paper only the pure crystalline white calcium or sodium salt is meant because it is well tolerated. Sorsby and Ungar (1947) showed that substantial concentrations of penicillin in the ocular tissues many times the usual therapeutic level can be obtained by the subconjunctival injection of crystalline penicillin in a dose of 50,000 units and that adequate levels persist for 6 hours. Sorsby and Reed (1947) subsequently elaborated their method of local penicillin therapy in cases of hypopyon formation by 12 to 16 sub-conjunctival injections of 50,000 units every 6 hours, followed by the 4 hourly instillation of penicillin ointment in a concentration of 100,000 units per gram. Among their group of 66 cases with hypopyon, there were 39 cases of infected corneal ulcers.

These authors made a detailed analysis of these cases of infected corneal ulcers with hypopyon treated by different methods of local penicillin therapy. They show subconjunctival injections to be the method of choice. It was successful in 18 out of 21 cases so treated. In three patients subconjunctival injections of penicillin proved inadequate and general sulphonamide therapy was applied. This

method of penicillin therapy by subconjunctival injections every six hours cannot be applied except in hospitals with resident doctors who can give the injections by night. Moreover as it entails the use of 200,000 units per day, it cannot be said to be economic. But there is no doubt that it is the most efficient method.

For general penicillin therapy the use of penicillin in oil and beeswax has greatly reduced the number of injections so that two injections can be given daily. The question, as to whether the same material can be used subconjunctivaly twice daily, arises. Sorsby and Ungar (1946*b*) found by animal experiments that such a procedure gave a high and sustained level of penicillin, but it was clinically inapplicable in ocular affections as it produces a severe reaction with gross corneal damage.

It was by chance that I was forced to try the use of two injections of penicillin daily. During the summer of 1947, a shortage of the supply of penicillin occurred in Egypt, and it was very difficult to get it except for few patients after complicated procedures. Under such a condition, extreme economy in the use of penicillin was necessary. The first case in which subconjunctival injections of penicillin were used by me is worth being reported in detail as it impressed upon me the efficiency of subconjunctival injections twice daily, as well as its superiority over some other methods of local penicillin therapy.

Case Report with Comment

On 18th July, 1947, M.S., a male rural infant, aged 18 months, was brought to my clinic by his parents. There was a history of typhoid fever of one month duration, towards the end of which he became very thin and developed an opacity in the right eye since four days ago and in the left eye since two days ago. On examination, he was found to be very emaciated, but there was no fever, and apart from his eyes, there was no other abnormality. The right conjunctiva was injected. There was a large deep ulcer in the right cornea, which occupied almost all the lower half of the right cornea and encroached on the upper half, covering the whole pupillary area. Its base was dirty, sloughing and thin and there was a severe hypopyon occupying about one quarter of the anterior chamber. The left conjunctiva was injected. There was an ulcer in the lower part of the left cornea occupying about one sixth of the corneal surface. No hypopyon existed in the left eye.

General treatment by the appropriate diet, vitamins and tonics was carried out by a paediatrician.

It was evident that the right eye was in a most serious state and there was a great danger of its being lost. In an attempt to save the right eye, I decided to use penicillin in this case, and to use it

economically as there was a great shortage of this drug at that time. An amount of 10 c.c. of distilled water was put in a bottle of 100,000 units of crystalline penicillin; 3 c.c. of the solution were taken, and diluted with 9 c.c. of distilled water so that a solution containing 2,500 units per c.c. was obtained, and this was used as drops for both eyes after a preliminary wash of the eye. The treatment started at about 10 a.m., and consisted of the instillation of two drops of that solution in each eye every minute for the first half-an-hour, then every five minutes for the next half-an-hour. At the end of the first hour, the left ulcer improved, and its base became clearer. The improvement in the right ulcer was dramatic. Its base which was very dirty, became clearer to a marvellous extent. The application of drops for the first hour was carried out by the nurse, but after this first hour, I sent the patient home with instructions to his parents to instil the drops every half-an-hour. At 7 p.m., I saw the patient again and the condition of both ulcers was as bad as when first seen. The parents denied any neglect, but probably there was gross neglect, as the type of parents, who bring their child to medical treatment only when the disease is far advanced, are usually negligent. It is equally possible that in this case half-hourly instillations of penicillin drops were not adequate. Again I repeated the instillations just as in the morning, every minute for the first half-an-hour, then every five minutes for the next half-an-hour. Again the same marvellous improvement occurred, and again I sent the patient home with instructions to use drops every half-an-hour as long as either of his parents could keep awake by night, noting that penicillin in oil and beeswax for systemic administration was not available. Next morning both eyes were seen to be as bad as when first seen. It seemed that though the case responded well to penicillin, some change in the mode of administration must be made. Probably half-hourly instillations at home were not adequate but more frequent instillations were very tedious to the attendants and did not seem to be practical. Probably some neglect in following the instructions was responsible for the failure. Subconjunctival injections seemed to offer a mode of treatment which the attendants could not affect by their neglect. These had to be carried out twice daily, as I could not give them more frequently with convenience. 0·5 c.c. of the solution already prepared in the bottle was injected twice daily in each eye. This amount contained 5,000 units of penicillin. Seven subconjunctival injections were given in each eye over a period of three and a half days. Rapid and progressive improvement was noticed during this short course. Apart from atropine ointment twice daily no other treatment was applied locally.

Towards the end of the course the base of each ulcer was quite clear and the right hypopyon disappeared. Owing to the shortage of penicillin no more injections could be given. Lamellae of penicillin,

each of 250 units, and penicillin ointment of a concentration of 1,000 units per gram were prescribed and were ordered for use every hour alternately. They were used during daytime and most of the night, and the application was made by the mother at home. Twenty-four hours from the onset of the use of lamellae and ointment, the base of the ulcers on both sides became gray and infiltrated.

This indicated that penicillin injections should be resumed, but no crystalline penicillin was available for further injections. Two days later the right ulcer perforated with the formation of a small prolapse of iris. Rapid healing of the right ulcer followed the occurrence of the iris prolapse. Healing of the left ulcer occurred without prolapse.

The behaviour of the right ulcer seemed to show that lamellae and ointments of the concentration mentioned above are not so efficient as subconjunctival injections. Moreover the difficulty of their application safely in infants and young children, who often struggle during their application, renders their use at home unsafe in cases of ulcers with thin base because of the danger of inducing perforation. Also the possibility of neglect exists with such types of patients.

Further Development and Details of the Method of Subconjunctival Injection of Penicillin Twice Daily

The case mentioned above pointed to a method of penicillin administration which was practical, efficient and economic. It was worthy of further trials and attempts towards perfection.

Patients dislike subconjunctival injections and the majority object to them. Two instillations of 1 per cent. pantocaine solution at three minutes intervals while the eyes are closed are harmless to the epithelium and produce sufficient anaesthesia to allow the prick of the needle to be done almost painlessly.

Apart from the prick of the needle, the mere infiltration of fluid under the conjunctiva causes some pain while the fluid is actually passing and for some time afterwards and this pain can be easily abolished if 1 per cent. novocaine solution in non-pyrogenic distilled water is used instead of simple distilled water in the preparation of penicillin solution.

A concentration of 20,000 units per c.c. was found to be quite satisfactory in cases where 10,000 units per c.c. was not quite satisfactory. Therefore to a bottle of 100,000 units of crystalline penicillin salt, 5 c.c. of 1 per cent. novocaine solution in distilled non-pyrogenic water was added, and 0·5 c.c. was injected subconjunctivally twice daily, at about 9 a.m. and 8 p.m., each injection being given after two instillations of 1 per cent. pantocaine solution. The eye is opened and partially fixed by a pair of Desmarres' retractors applied to the lids with their tips introduced into the fornices if the patient is unable to open and fix his eye while the injection is being given subconjunctivally at a distance of 2 to 3 mms. from the limbus.

The use of Desmarres' retractors is specially valuable when the injection is given above the limbus. It is advisable to change the site of injection every time. Even in unsteady nervous children, the injections can be safely given. The trunk and hands are fixed by another nurse; the nurse holding Desmarres' retractors assists slightly in fixing the head by the same hands; and the doctor can use one hand for fixing the head while the other hand holds the syringe and gives the injection.

One bottle of 100,000 units is enough for a course of 5 days which is usually sufficient. The addition of adrenalin chloride solution to penicillin solution to render it less readily absorbable into the general circulation is liable to destroy the penicillin especially because of the long period of 5 days over which the acid adrenalin chloride acts on penicillin while it is in the bottle until it is completely exhausted. The destructive effect of solutions, even of poor acidity on penicillin was demonstrated by Garrod (1945). Therefore no adrenalin chloride solution, which is acid, may be added to penicillin solution (Cameron 1945).

One course of 10 injections is usually sufficient for almost all cases. At the end of the course the healing of the ulcer is progressing well, and it is quite sufficient to use frequent wash and hot fomentations after stopping the injections. If the slightest sign of infiltration recurs, the course may be repeated partially or completely according to the discretion of the oculist

In addition to penicillin injections, atropine ointment 1 per cent. twice daily is applied as a routine in all cases, except in eyes predisposed to glaucoma.

No other local or general treatment was applied in the majority of cases as long as the injections were given. But frequent wash and hot fomentations were used after the course was completed.

In a small proportion of cases, the improvement produced by the first few injections was slight. In them the use of frequent wash, hot fomentations and local sulphadiazine ointment 5 per cent. every two hours, in addition to subconjunctival injections of penicillin, helped to accelerate cure.

It may be noted that in general medical practice some practitioners dislike the use of penicillin in oil and beeswax, and use massive doses of penicillin in water two or three times daily with good clinical results. The success of subconjunctival injections twice daily runs parallel with the success of massive doses of aqueous solutions of penicillin administered twice or thrice daily in general medical practice.

If there is muco-purulent or purulent discharge in the conjunctival sac in cases of corneal ulcers, subconjunctival injections of penicillin should not be administered before the discharge is controlled by

penicillin drops in the mode suggested by Sorsby for ophthalmia neonatorum. A solution of crystalline penicillin of a concentration of 2,500 units per c.c. is prepared. Two drops are instilled into the eye every minute for the first half-an-hour, then every five minutes for the next half-an-hour. At the end of half-an-hour, the discharge practically ceases in penicillin sensitive cases, but the drops should be continued every five minutes for another half-an-hour. Then subconjunctival injections can be started. If the discharge is resistant to penicillin drops, subconjunctival injections are contraindicated for obvious reasons. The micro-organism causing the ulcer is that of the associated conjunctivitis and as the discharge causing the conjunctivitis is not controlled by penicillin, the micro-organism is penicillin resistant and no useful purpose is served by subconjunctival injections. Moreover there is obvious danger of deep infection in the orbit. Fortunately, cases of conjunctivitis with severe ulcers of cornea are usually sensitive to penicillin.

Comparative Value of this Method

No attempt is made to compare the therapeutic value of the method of subconjunctival injections of penicillin twice daily with the method of subconjunctival injections every six hours. The practical disadvantages of the latter method have already been mentioned.

A comparison between this method of two subconjunctival injections of penicillin daily as detailed above and the routine older methods of treatment without penicillin is to be considered.

In pre-sulphonamide days the routine treatment of infected corneal ulcers was by frequent wash, hot fomentations and atropine ointment. To these, foreign protein therapy was very frequently added. Milk injections are the form in which foreign protein is usually administered in Egypt. Ten c.c. of sterile milk are administered intra-muscularly every other day. A course of 2 to 5 injections is usually given. Milk injections usually cause rapid clearing of infected corneal ulcers, but very frequently ulcers grow much deeper and even perforate while milk injections are administered, and ophthalmologists in Egypt believe that this increase in depth, and even perforation, are provoked by milk injections.

General sulphonamide therapy formed a substitute for milk injections and was used in addition to frequent wash, hot applications and atropine ointment. Sulphathiazole was administered in doses of one gram. four or five times daily. This treatment could not control the progress of the ulcer for 2 or 3 days or even more. Severe ulcers frequently perforated in spite of this treatment.

Penicillin therapy, in the method detailed above, has the great value of immediately controlling and stopping the progress of the

ulcer from the first injection. Then the base and margins of the ulcer quickly get progressively clearer, and gradually healing occurs. Only severe infected ulcers of the cornea were selected for this form of therapy. Milder forms of corneal ulceration were excluded as they responded rapidly to older methods of treatment. The severe cases selected for penicillin therapy were 26 in number. Some of them were traumatic with or without hypopyon but most were secondary to purulent conjunctivitis and a few were secondary to mucopurulent conjunctivitis. Most of them responded rapidly, almost immediately to subconjunctival injections of penicillin as detailed above. The progress of the ulcers was stopped after the first injection, then the base and margins became clearer and progressive healing followed.

Few cases showed slight response and the improvement produced by the first few injections was slight. In them penicillin can be said to be inadequate and the use of frequent wash, hot fomentations and local sulphadiazine ointment 5 per cent. every two hours during daytime, in addition to subconjunctival injections of penicillin helped to accelerate cure. Not a single case of perforation occurred in this series of 26 cases of severe infected corneal ulcers.

Conclusions

This method of treatment yields better results than the older methods of treatment in which general sulphonamide therapy or foreign protein therapy formed a part of the treatment. This claim is supported by general clinical observation as mentioned above, but no comparative statistics were made. This method is considered to be a practical, efficient and economic mode of penicillin administration in severe infected corneal ulcers.

Summary

A method of treatment of severe infected corneal ulcers by subconjunctival injections of penicillin twice daily is described.

The value of this method compared with the older methods of treatment is discussed. This value is demonstrated by general clinical observation but no statistics were made.

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OPERATION FOR PERSISTENT PUPILLARY MEMBRANE. NOTES ON A CASE*†

BY

ZOLTÁN BÁTHORI

BUDAPEST

SINCE the use of the slit-lamp the diagnosis of persistent pupillary membrane has become very frequent, and even the smallest vestige of the condition can easily be recognised. It may appear in a variety of forms and though the condition is frequent (according to Staehli 31 per cent. of all cases) it is extremely rarely that it interferes with the patient's vision, or that an operation has to be done to improve sight.

The first operated cases were published by Wiegmann (1916). He operated on four eyes of a pair of twins, and after several repeated operations the vision improved. Mawas and Terrien (1922) refer to a histological examination of a persistent pupillary membrane which was removed by operation and in this case too vision had improved. In a case of Noji (1930) optical iridectomy was performed as the persistent pupillary membrane was adherent to the lens capsule and partial lenticular opacities were present. A good result was achieved. Nakame (1937) refers to several operated cases. It is interesting that in spite of the number of reported cases text-books of ophthalmology, or of operative eye surgery do not describe an operation for the condition.

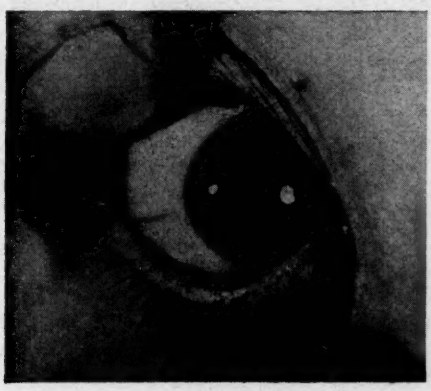

FIG. 1.

* From The Eye Clinic of Pázmány Péter University, Budapest, (Director: Prof. Joseph Imre.)

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In 1934 I presented a patient to the Hungarian Ophthalmological Society with a dense persistent pupillary membrane occupying the whole area of the pupil (Fig. 1.).

30 years old woman, had always poor vision. She noticed recently further deterioration. V.A. R.E. Counting Fingers 3m. −3·0 D.sph. 5/50.
L.E. 5/30 −3·5 D.sph. 5/12.

Nystagmus of small amplitude, mainly in the horizontal direction.

R.E. The pupillary area was occupied by a mass of brownish tissue, identical in colour with the iris, slightly prominent. With the slit-lamp it showed a dense central part of 1·5mm. diameter, and from here a mesh of threads of different thickness originated, passing in radial direction towards the iris crypts. The pupillary margin could be seen through the mesh, and the pupil was active. The lens appeared clear.

L.E. showed a similar but less marked picture. The central dense mass was of only 0·5mm diameter. Lens, media and fundus showed no abnormal changes.

Operation on the right eye was performed by Professor Imre.

After a keratome incision the filaments were pulled into the wound, one by one, with a small iris hook and severed with de Wecker's scissors, and eventually the whole persistent pupillary membrane was removed. After operation the whole area of the pupil was clear

FIG. 2.

(Fig. 2.) and vision had improved with glasses to 5/8. The left eye was not operated upon.

We think that in cases where the vision is reduced by persistent pupillary membrane an operation is indicated, and the operation of choice is:

(1) as above described, if the persistent pupillary membrane is free and not adherent to the lens capsule, or

(2) an optical iridectomy if it is adherent to the lens capsule.

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ANNOTATION

Dislocated Lenses

The lens may be dislocated either forwards or backwards by direct or indirect violence. We remember a case in the latter category in a patient of many years standing. On his first visit he was wearing a medium myopic correction with the stronger glass in the right side. He had a cataract in this eye, the other lens being clear and vision corrected to 6/6 and J.1. The right eye had perception and projection of light and as far as we could see there were no keratic precipitates. This patient visited us for about twenty years at regular intervals. On no occasion could we see any precipitates, but we could never feel quite sure that the condition had not arisen in consequence of some low grade inflammation: and as he was used to his restricted field of vision and had good vision in the other eye we refused to suggest an operation.

This patient about eighteen months before his death had a slight accident. He slipped on his own doorstep and sat down rather heavily. Soon after, he called to say that he could see more light than usual in his bad eye. The upper margin of his lens was visible in the upper part of his pupil and by degrees the lens vanished into the bottom of his eye and vision of 6/18 could be obtained with a suitable lens; but he was not happy and preferred to wear a black patch on the right side. When he died, in his 80th year, the lens was still in the depths of his eye.

On only one occasion were we called upon to deal with a lens dislocated into the anterior chamber. This was in an old man who had been an out-patient for many years. He was a marked case of interstitial keratitis and his left cornea was so much scarred and flattened that the eye was useless. The right eye had very poor vision, not more than hand movements. The family had been celebrating Christmas and the two sons became quarrelsome. In trying to separate them the patient received a heavy blow with a fist in his right eye and the lens was dislocated into the anterior chamber. We dealt with it in the usual way under a general anaesthetic. A needle was passed into the dislocated lens from the limbal area, to fix the lens and given to the house-surgeon to hold, a keratome section was made and the lens extracted with a vectis. He left hospital with perception of light and we did not see much more of him.

OXFORD OPHTHALMOLOGICAL CONGRESS 1948.

THE 34th annual meeting of the Oxford Ophthalmological Congress was held on July 8th., 9th. and 10th. The increasing popularity of this conference necessitated a change of venue, and this year the congress was housed in Hertford College, while the proceedings were conducted in the School of Geography since the theatre of the School of Human Anatomy could no longer offer sufficient accomodation.

The Master, Mr. F. A. Williamson-Noble, opened the congress on Thursday morning with an address of welcome. After this Dr. Arthur Greene made a presentation to Dr. F. A. Anderson, on his retirement as secretary of the congress, of a cheque subscribed by members in token of their appreciation of his untiring efforts and notable success in forwarding the interests of the congress for the past 12 years. Dr. Anderson expressed his thanks and the pleasure he had derived from his work as secretary.

The subject for discussion, "the use and abuse of topical ocular therapy," was opened by papers by Mr. F. Ridley, Dr. F. E. Preston and Dr. J. M. Robson. Mr. Ridley drew attention to the tear-film and described its anatomical position and physical properties. He emphasised that lyzozyme normally kills all airborne bacteria and also the common pathogenic organisms, and that it is destroyed or inhibited by drugs containing free halogens and by acriflavine. The lyzozyme content is reduced in interstitial and phlyctenular keratitis, and is increased by the use of atropine in these diseases, and a return to a high level presages the recovery of the patient. In the use of drugs in the conjunctival sac dilution occurs rapidly, and few drugs retain an effective concentration for long. Solutions are diluted by half every 45 seconds, but emulsions are retained longer. The latter should, when possible, be emulsion of oil in water, not the reverse, and thereby an increased corneal permeability is obtained. With reference to atropine irritation the approximate ratios of solutions, lamellae and serum of atropine and hyoscine were indicated, showing that lamellae hyoscine were eight times less irritant than solution of atropine. Mr. Ridley considered that irritation could almost invariably be avoided by the use of lamellae. Local sensitisation was due to the presence of histamine-like bodies in the tears, which are neutralised by the normal aqueous, but this mechanism is defective in certain diseases.

Dr. Preston considered ocular therapy as of two schools, the empirical and the rational. He noted that the secondary effects of drugs may sometimes prove more valuable than those of their original purpose. He then gave a number of specific instances of valuable applications in particular conditions.

Dr. J. M. Robson spoke of the value of local application in obtaining a higher concentration than could safely be reached by systemic therapy. The limiting factor in the value of many drugs was the rapidity of local elimination. He mentioned four methods of overcoming this difficulty by (1) iontophoresis, (2) deturgescent agents, (3) subconjunctival injection, (4) intra-vitreous injection. He considered that deturgescence of the cornea had been neglected clinically, and remarked that subconjunctival injection should be combined with vaso-constriction.

In the subsequent discussion the influence of allergy was referred to by Dr. Vera Walker, the value of powders by Dr. Traquair, injection into the anterior chamber by Dr. Huber, and the abuse of penicillin by Mr. J. P. F. Lloyd.

In the afternoon, Dr. J. J. Healy read a paper on "unusual ocular injuries," and members contributed a number of equally surprising experiences.

After this, Dr. Grant Peterkin contributed an interesting paper on "dermatological conditions affecting the ocular adnexa." He divided the conditions under review into (*a*) new growths, (*b*) oedematous swellings of the lids, (*c*) Tuberculosis cutis and allied diseases, (*d*) Systemic diseases; his discriptions were accompanied by numerous coloured illustrations. He laid stress on the frequency of contact dermatitis in many obscure cases of lid swelling and mentioned the characteristic features. His experience with acne rosacea had been variable and often disappointing. He had noted much dermatitis from the superficial application of sulphonamide and penicillin ointments and creams.

Mr. Dickson Wright then read a paper on the "approach to orbital tumours" in which he advocated a wide exposure from the lateral side with temporary removal of up to 1/3 of the orbital margin. This was replaced at the end of the operation and always took well with no tendency to absorption. A film was shown of the operative technique in two cases. Mr. H. B. Stallard also showed a film of the Kronlein operation and Mr. J. Foster gave the results of his own experiences with such cases.

On Friday, Mr. F. W. Law reported an unusual "case of retinoblastoma" in which the following points were notable, (1) The involvement of the second eye while under observation. (2) The apparent total destruction of the focus in this eye by diathermy. (3) Death by distant metastasis, though both optic nerves were apparently normal during life.

Mr. F. Ridley then gave a paper on "contact lenses" and dealt with recent developments in theory and practice. Improved methods of moulding were described and also a simplified method for accurate estimation of the curvatures required for correction. Veiling, caused

by the development of negative pressure and swelling of unsupported tissues by the action of lid pressure, could be relieved by the inclusion of channels at the lower end of the lens leading into the tear pool in the lower fornix. Photophobia, closely related to veiling, was more difficult to deal with, but tinted glasses would often help.

Dr. Z. A. Leitner described the value of Grenz rays in ophthalmology. Having only minimal penetrating power they were specially safe for the treatment of superficial lesions; 98 per cent. of the rays are absorbed before reaching the lens. Success has been obtained in the treatment of corneal ulcer, recurrent erosion, superficial punctate keratitis, and phlyctenular keratitis. Mooren's ulcer did not respond to Grenz ray therapy, and acne rosacea keratitis in some cases only.

The Doyne Memorial Lecture, delivered by Sir Stewart Duke-Elder under the title of "The Blood-aqueous barrier," described the latest work on the problem of the intra-ocular fluid. By the use of neutrons tracer elements could be added to substances and, by their radio-activity, their course after intravenous injection could be followed in the ocular tissues, and much less disturbance from the normal was possible in the animals used. The presence of β. particles in the aqueous was the basis of the examinations. From these experiments it appeared that water is derived by simple diffusion at a rate of 50 cu. ml. per minute and that the mechanism in Schlemm's canal is one of bulk flow. Water diffusion into the vitreous is 1/5 the rate into the anterior chamber. Sugars reach the anterior chamber by simple diffusion, but the lower ratio in the vitreous argues an additional chemical barrier to this tissue. Experiments showed that sugar is metabolised in the eye chiefly by the lens and the retina. Nitrogenous substances did not enter the aqueous so well and also were affected by the vitreous barrier, while electrolytes, with the exception of phosphate, gave similar values to sugars. Sodium, potassium and chloride reach the posterior part of the eye solely through the ciliary body and pass the vitreous barrier slower than sugars *vis-a-vis* their molecular size.

The lecturer postulated a variation of the mechanism of transference in different parts of the eye. These recent experiments lead the lecturer to the conclusion that the capillary cells, not the interspaces, constitute the sole barrier and that these cells show variations in selective porosity. There seems however to be evidence that the ciliary epithelium in addition actively engages in the secretion of sodium chloride.

At the conclusion the Master presented Sir Stewart Duke-Elder with the Doyne Medal.

A discussion on the "operative treatment of glaucoma" was opened by Mr. Williamson-Noble and Mr. Maurice Whiting. The

Master revealed a catholic variety of choice with a preference for iridectomy or iris inclusion in acute congestive, and cyclodialisis or iris inclusion in non-congestive cases: for buphthalmos he commended goniotomy. In association with aphakia he had found trephining less disappointing than cyclodialysis, and thought a small flap sclerotomy worthy of trial in thrombotic glaucoma. He also gave a number of practical suggestions for pre- and post-operative treatment.

Mr. Whiting reviewed the indications for operation in chronic cases. He preferred trephining for most cases in spite of admitted drawbacks, with a preference of Herbert's sclerotomy as an alternative.

Dr. F. A. Anderson mentioned the value of intravenous sucrose injections as a pre-operative measure, and described the technique of iris inclusion without introducing instruments intra-ocularly.

Dr. Traquair described his pilgrimage from trephining to cyclodialysis, thence to cyclodiathermy, and his final return to the trephine as the operation of choice.

Mr. E. G. Mackie was a frank advocate of iris inclusion and gave comparative figures of his results showing a high proportion of success.

Mr. A. G. Palin on the other hand favoured the trephine.

Mr. A. MacRae had come to prefer the modified iris inclusion operation described by Greenwood and Eggers, and gave illustrations of the technique together with a table of results.

Many other members took part in a free discussion which continued till the adjournment for tea.

On Saturday, Professor Loewenstein (Glasgow) demonstrated his theories on the anterior drainage system of the human eye by a series of beautiful slides. Mr. J. Minton (London) discussed occupational diseases of the eye in the glass and metal industries, caused by the short infra-red rays, incidentally showing the enormous decrease in glassblowers cataract since the introduction of automatic machinery in the bottle industry, and the high incidence of cataract among chain makers which is still a manual industry. Dr. Gunnar von Bahr described a method of accurate measurement of the thickness of the living cornea and its variations in response to solutions of varying osmatic pressure. His experiments supported the theory of Cogan and Kinsey bearing on the circulation of fluid in the cornea and its purpose in its metabolism. Dr. Winifred Fish (Oxford) read a paper on "hereditary mesodermal dystrophy," and Miss Margaret Dobson (London) on "dynamic retinoscopy."

FACULTY OF OPHTHALMOLOGISTS

The following have been elected as Officers of the Faculty for 1948-49 :—

President: Sir Stewart Duke-Elder; *Vice-President*: Mr. J. J. Healy; *Honorary Secretary*: Mr. Frank W. Law; *Honorary Treasurer*: Mr. O. M. Duthie.

The following Standing Committees and Sub-Committees have been elected :—

Constitution: Mr. F. A. Juler (Chairman and Convener), Mr. George W. Black, Mr. J. J. Healy, Mr. W. H. McMullen, Professor W. J. B. Riddell; *International Relations*: Mr. F. A. Juler (Chairman and Convener), Mr. R. C. Davenport, Mr. J. H. Doggart, Miss Ida Mann, Professor W. J. B. Riddell; *Medico-Political*: Mr. J. D. M. Cardell, Mr. J. H. Doggart, Sir Stewart Duke-Elder, Mr. P. Jameson Evans, Mr. R. Affleck Greeves, Mr. J. J. Healy, Mr. E. F. King, Mr. Frank W. Law, Mr. E. G. Mackie, Dr. John Marshall, Mr. A. S. Philps, Mr. J. N. Tennent, Mr. David Wilson; *Education and Research*: Mr. R. C. Davenport (Chairman and Convener), Mr. J. Foster, Mr. E. F. King, Mr. T. Keith Lyle, Miss Ida Mann, Professor W. J. B. Riddell, Dr. George Scott.

The Officers are *ex-officio* members of all Committees.

Representatives of the Faculty on the Prevention of Blindness Committee, National Institute for the Blind: Mr. J. H. Doggart, Sir Stewart Duke-Elder, Mr. Humphrey Neame, Mr. D. Stenhouse Stewart, Mr. Maurice Whiting; *Representatives of the Faculty on the Ophthalmic Group Committee, British Medical Association*: Mr. J. D. M. Cardell, Mr. J. H. Doggart, Mr. R. Affleck Greeves, Mr. E. F. King, Dr. R. S. MacLatchy, Mr. J. N. Tennent.

Mr. J. H. Doggart has been co-opted to the Council of the Royal College of Surgeons of England for 1948-49 as the representative of the Faculty.

Representatives of the Faculty have met representatives of the Ministry of Health to discuss several points connected with the Supplementary Ophthalmic Service, including the use of drugs by opticians. The Ophthalmic Benefit Approved Committee have recently authorised the use of certain drugs by opticians in National insurance work. The Faculty's representatives have made it clear that they are strongly opposed to the use of drugs by opticians, and the Ministry officials, while not committing themselves, have suggested that for the Supplementary Eye Service no regulations about the use of drugs by opticians should be laid down, but that a Commission, which has been appointed to consider registration of opticians, should make a decision on the matter. The standard of vision required on examination by opticians and the need for a report to the patient's general medical practitioner if that standard

was not attained has also been considered. The Faculty's representatives put forward the opinion that 6/6 for each eye examined should be the standard. The Ministry officials considered that this would be too high a standard for incorporation into regulations, and agreed that guidance on this matter should be given in a handbook to be issued to opticians, the relevant portion being first submitted for the Faculty's comments.

The question of whether ophthalmologists should see patients in their own consulting rooms under the Supplementary Ophthalmic Service has been discussed by the Council. It is the policy of the Faculty that state patients should be seen in Clinics under the Supplementary Service or in Hospital Clinics under the Permanent Service, and that this latter Service should be inaugurated as soon as possible, because it is the Faculty's view that no Supplementary Ophthalmic Service Clinic should take place in Hospital. Where there is no Clinic available, it will presumably be unavoidable for patients to be seen in private consulting rooms under the Supplementary Ophthalmic Service though it is likely that this practice will result in a destruction of private practice.

Nominations for Ophthalmic Services Committees of Local Executive Councils throughout the country have been discussed with Mr. Grey Turner of the British Medical Association. Various fusions, modifications and additions have been agreed, which will all appear on the final list.

BOOK NOTICES

Modern Trends in Ophthalmology. Edited by A. SORSBY. 600 pages. 169 figs. London, Butterworth & Co., 1948. Price 63/-.

The second volume of "Modern Trends" follows on the lines of its predecessor and is equally good. Forty-eight articles are included, arranged in sections—physiology, diagnostic procedures, pathology, treatment and social aspect of ophthalmology. They touch practically every aspect of the specialty which has shown progress during recent years and at the same time fill a number of gaps left in the previous volume. The editor has drawn widely from many countries for his contributors among whom are to be found many from most countries of Europe and America. Not only has the choice been wide but it has also been good. Able and impartial editing is seen in the readability of all the sections, the exclusion of well-established information and the inclusion of only new points of view. The volume will be found most useful to those wishing a short resumé of recent progress.

Introduction to Physiological Optics. (Einführung in die physiologische Optik). By A. v. TSCHERMAK-SEYSENEGG. 2nd Edition. 213 pp. Springer, Vienna. 1947.

On certain aspects of the physiology of the eye v. Tschermak may be ranked as the greatest living authority, in particular on such abstruse problems as torsion and its perspective distortion of an after-image following movements of the eye, and perhaps more so on space perception; it is therefore of value to have, within the span of two hundred odd pages, a concise summary of present day knowledge of these aspects of physiological optics. The book also contains disquisitions on other branches of the subject: visual acuity, adaptation, after-images and colour vision including colour-blindness. In these last-mentioned sections the author seems not to have been able to draw to any great extent on the wealth of material in the British and American literature of the past ten to fifteen years (Hecht, for example, is barely mentioned; Hartline not at all); the book is thus very little more than a restatement of the author's earlier contributions to Bethe's Handbook. Valuable as these contributions were at the time, their main use now is as a source of references to the classical work and it may be that the author has been unwise in attempting to abridge them so as to bring them within the compass of this small book. If, instead, he had expanded his treatises on the eye movements and space perception and had provided also a thoroughgoing analysis of image-formation by the eye and its aberrations, the book would have been transformed into one of real value for the modern reader; as it is, the abbreviated accounts of these subjects are very difficult indeed to understand. The book contains references only to the author's earlier reviews on physiological optics to which the reader is referred for individual references to the literature.

OBITUARY

HENRY SMITH, C.I.E., Lieut.-Col., I.M.S., ret.

THE death of Lieut.-Col. Henry Smith in Ireland was announced in March, 1948. He was 91 years of age and few of his contemporaries can now be left alive. Smith received his medical education in Ireland and qualified M.D., M.Ch., in 1888.

In the early years of the present century the name of "Jullundur" Smith was on all ophthalmological lips. His enormous experience in cases of cataract in India led him to devise the intracapsular operation of extraction and in this he did pioneer work.

The advantages to the Indian peasant were obvious:— only one stay in hospital, one operation, no return for needling; and with so many illiterate patients; a glass for general use could be ordered almost as soon as the eye was white. In successful cases the surgeon was relieved of the bugbear of tags of capsule left to be incarcerated in the healing wound. Loss of vitreous was the item around which most of the criticism of this new operation centred.

Smith made a large section in the corneo-scleral junction; he cut no conjunctival flap; he performed a large iridectomy and delivered the lens by pressure on the lower part of the cornea with the blunt tip of a strabismus hook. The suspensory ligament was ruptured in the first place and the lens either "tumbled" or pushed straight out. In Smith's hands the results were good. He always insisted on the importance of having a properly trained assistant and spent much time and trouble in training his own.

Outside India the ophthalmological fraternity was critical of the operation. Surgeons in England, in particular, were concerned at the large loss of vitreous that sometimes occurred. When the writer first went to Moorfields as a clinical assistant he got the impression that the intracapsular operation was considered unjustifiable in view of the grave risks involved.

Smith was quite unperturbed by this criticism and went on with his work. He introduced a hook for the lens delivery in certain cases, published many papers in the *Lancet*, *Ind. Med. Gaz.*, and *Brit. Med. Jl.*, and summed up his experiences in a monograph on the treatment of cataract.

As time went by modifications were made in the operation, notably that of Barraquer, of Barcelona, who employed a suction pump for the lens delivery and nowadays the operation of intracapsular extraction is performed all over the world. The credit of this must go in the first place to Henry Smith for his pioneer work.

After leaving Jullundur, Smith worked as Civil Surgeon at Amritsar until he retired from the service and came to live at first at Sidcup, and later in Ireland.

The writer remembers Smith visiting Moorfields about forty years ago. He was a large man, with a massive head and not very approachable to juniors. Of our contemporaries who visited India to work with Smith we recall Basil Lang, who was greatly impressed by his stay at Amritsar.

NOTES

Appointments

MR. JAMES H. DOGGART has been co-opted a member of the Council of the Royal College of Surgeons of England for the ensuing year to represent Ophthalmology.

Mr. R. J. Buxton, M.B., has been appointed ophthalmic surgeon to the Yeovil District Hospital.

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American Ophthalmological Society: Officers

THE American Ophthalmological Society elected new officers at its recent meeting at Hot Springs, Virginia, for the current year: *President*—Dr. Bernard Samuels, New York; *Vice-President*—Dr. Parker Heath, Boston; *Secretary-Treasurer*—Dr. Maynard Wheeler, New York.

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Blindness in British African and Middle-East Territories

A REPORT of a joint committee appointed by the Colonial office and the National Institute for the Blind, following the visit of a Delegation to Africa and some Middle-East Territories between July, 1946, and March, 1947, has been published and can be obtained from H.M. Stationery Office.

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Back Numbers of the Journal

THE British Journal of Ophthalmology requires copies of the Journal for January, 1942, August and October, 1946, in good condition. Anyone having spare copies to dispose of should inform the manager.

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The Illuminating Engineering Society.

THE following officers for the next session are announced:—*President*—Mr. J. M. Waldram; *Vice-Presidents*—Dr. E. C. Walton, Mr. E. W. Murray, Dr. J. N. Aldington; *Hon. Treasurer*—Mr. J. G. Holmes; *Hon. Secretary*—Mr. H. C. Weston; *Hon. Editor*—Mr. W. R. Stevens.